ROYAL COMMISSION ON MATTERS OF HEALTH AND SAFETY

ARISING FROM THE USE OF ASBESTOS IN ONTARIO

VOLUME XXV A

INDEX OF WITNESSES:

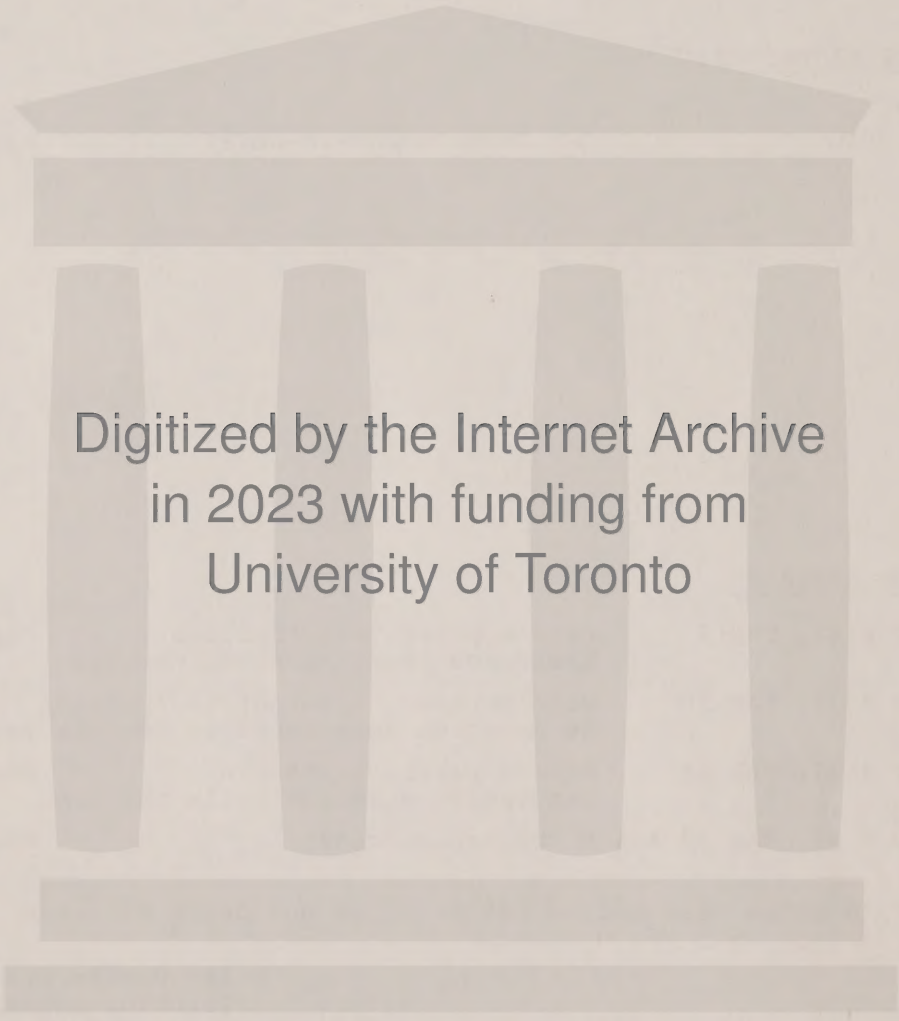


INDEX OF EXHIBITS:



REPORTER'S NOTE: See volume XXV B for second day's evidence

180 Dundas Street
Toronto, Ontario
Wednesday,
July 29, 1981



Toronto, Ontario
Wednesday,
July 29, 1981

Volume 25 A

THE FURTHER PROCEEDINGS OF THIS INQUIRY RESUMED PURSUANT TO ADJOURNMENT

APPEARANCES AS HERETOFORE NOTED

DR. DUPRE: Good morning, ladies and gentlemen.

Counsel, are there any matters that you wish to raise before I greet the witness?

M. CASGRAIN: Mr. Chairman, I do.

DR. DUPRE: M. Casgrain?

M. CASGRAIN: I understand, Mr. Chairman, that at some time it had been suggested that perhaps this Commission and other people who are participating in the work of this Commission might eventually consider an invitation to visit one or two of the mines in Quebec, which I think would be of interest to the Commission and all those concerned.

I think this is a propitious time to ask whether you would be interested in so doing, and if so, before the winter sets in. At least, you know...we have a nice winter in Quebec, but I think you would love our asbestos better in the summer than in the winter, and I suggest that perhaps you might wish to visit either one mine in Asbestos, or one in Thetford, or either of the ones, and I am completely open.

I'm making the invitation on behalf of the QAMA, and I'm suggesting that perhaps two mines could be made available

M. CASGRAIN: (cont'd.) to you. Again, Asbestos was an idea of mine, and one in Thetford, perhaps Lake Asbestos.

So I'm putting it forward, and if you think, if the Commission accepts, we would be delighted to...we invite the whole staff and all those here who are concerned with the Inquiry. We will make necessary arrangements in due course, but we do need a little time to so arrange.

I suggest you might be one day. You could visit one mine in the morning and one in the afternoon, and eventually we would make sleeping accommodations somewhere around there.

Travelling arrangements and so on would require perhaps two days.

DR. DUPRE: Thank you very much, M. Casgrain. As, of course, you are aware, we have had under advisement a very kind invitation from the QAMA for some time, and certainly your seasonal point is well taken.

As I had to mention at one stage of the game yesterday, I am told the Commission has a somewhat better handle on what its exact fate is going to be in the month of August. We have to keep the possibility of site visits or other things under advisement, but I appreciate your point. We are continuing to hold the invitation under advisement.

Any other matters?

MR. LASKIN: I don't believe so, Mr. Chairman.

DR. DUPRE: Well, may I, on behalf of all of you, greet most warmly Mr. Julian Peto, who has come from the land of magic weddings to be with us to give sworn testimony as an expert witness.

Mr. Peto, your reputation preceeds you, sir. You are most welcome here, indeed.

Miss Kahn, would you swear in the witness, please?

JULIAN PETO, AFFIRMED

EXAMINATION-IN-CHIEF BY MR. LASKIN

MR. LASKIN: Mr. Peto, before you begin, let me tell you that in front of you in that red binder are copies of your articles which, for our purposes, we put in one volume and we have given it an exhibit number for our record, which is exhibit thirty-seven, and so if we refer to any article it will be by the tab number in that red book.

Just let me deal with the additional materials that you gave me which aren't in the book, and I distributed three articles by Mr. Peto. I take it none of these...all of these are recently written articles which have not as yet been published, is that correct?

THE WITNESS Yes. The report to the EPA won't be published as such. It's on the public record, I think, but it isn't to be published formally.

MR. LASKIN: The first one, entitled Mesothelioma Incidence Among Asbestos Workers, Implications from Models of Carcinogenisis and Risk Assessment Calculations, let's call tab nine.

EXHIBIT #37, TAB 9: The abovementioned document was then produced and marked.

MR. LASKIN: The second, An Alternative Approach for the Risk Assessment of Asbestos in Schools, the report to the EPA, let's call tab ten.

EXHIBIT # 37, TAB 10: The abovementioned document was then produced and marked.

MR. LASKIN: Then finally, the paper you gave at Coldsprings Harbour, Trends in Mesothelioma Incidence in the U.S. and the Forecase Epidemic Due to Asbestos Exposure During World War II, let us call Exhibit eleven...tab eleven of exhibit thirty-seven.

EXHIBIT # 37, TAB 11: The abovementioned document was then produced and marked.

MR. LASKIN: Q. Now, I take it that the first thing that you are going to discuss with us is the work that you have done with respect to mesothelioma, and which is at least in part reflected in this paper with Drs. Seidmann and Selikoff?

THE WITNESS: A. Yes.

Shall I just talk briefly about the work that we have done on mesothelioma and lung cancer, because it forms the basis of...

Q. Why don't you.

A. ...what I was going to say.

The background to both mesothelioma and lung cancer in asbestos workers is this work which was done by Richard Doll in relation to lung cancer incidence in smokers. The lefthand graph shows the...these are logarithmics...this is the log of age and the log of incidence. They are straight lines on one of these graphs, the incidence is going up as a power line. So the slope of this line is actually four, so this means the incidence of lung cancer, in this case in nonsmokers, is going up as the four power of age.

The slope of this line is seven, so this means that the incidence of lung cancer in cigarette smokers is going up at the seven power of age.

Doll pointed out about ten years ago that in fact if you replot the same data, still plotting nonsmokers against age, but this time plotting cigarette smokers against duration of smoking, the two lines are parallel, so it turns out that this is some meaningless accident.

I mean, the meaningful analysis is this one, and what it shows is that the incidence of lung cancer rises as the fourth power of age in nonsmokers, and as the fourth power of

A. (cont'd.) duration of smoking in cigarette smokers. He suggested that this meant that the mechanism is in fact that same, that all you were doing when you smoked cigarettes was produce the exact same disease by exactly the same mechanism, but that everything was happening at a hundred times the rate.

Can I write this on the board, because it underlies and it's important...so the incidence of lung cancer is proportional to age to the power of four in nonsmokers, and duration of smoking to the power of four in smokers.

He further suggested, although you can't actually prove it directly from these data, that the incidence of lung cancer in smokers was actually unrelated to age, that this equation has nothing to do with age, and if you started smoking when you were forty, your incidence rises as a duration of since you started to smoke, and if you started at twenty, it rises the time that you started to smoke. So if you started smoking when you are twenty, your lung cancer thirty years later would be exactly the same as the lung cancer rate in someone who started at the age of forty, thirty years later.

Is that...is that clear?

In other words, that if you start smoking when you are twenty, your lung cancer rate goes up like that. And if you start smoking when you are forty, it goes up exactly the same way, just moves over twenty years. The cancer rate is completely unrelated to age, as such.

Q. But if you are a nonsmoker...?

A. If you are a nonsmoker, it starts at age nought, going up in the same pattern, but of course it's divided by a hundred. So it goes up in the same pattern, but instead of looking like that, it looks like that. It's the same shape, but reduced by a factor of a hundred.

That's the difference between these graphs, and the difference between here and here. The slope is the same,

A. (cont'd.) the pattern is the same, but it is reduced by a very large factor.

Q. Can I...maybe it's my lack of knowledge of statistics. Are you saying that if you are a nonsmoker with respect to lung cancer, I thought that that formula meant that your incidence rate depended on how old you were?

A. If you are a nonsmoker, yes. I mean this is age, starts at age nought for nonsmokers...starts at age nought and goes up in this pattern at the fourth power of age.

Presumably in smokers, what you actually have is duration of smoking to the fourth, plus age to the fourth times a very, very small factor. But the weight is so low in nonsmokers that you've got a negligible factor of lung cancers in nonsmokers.

Q. So the controlling factor is smoking?

A. Yes.

And this implies that cigarettes affect the beginning of the process, they affect the initiation process in lung cancer.

Q. Just for our own record, because I take it that particular transparency is not amongst any of the articles that you published...

A. In reference then, this thing about implications of mesothelioma incidence...tab nine discusses this and cites references to these data. It's in the references of that data.

MR. LASKIN: I wonder if we can just note for the record now that perhaps we will arrange a copy of the transparency and just circulate it amongst us so that we know what we are talking about.

THE WITNESS: Sure.

So anyway, Doll suggested that this meant that lung cancer rates had nothing to do with...in smokers...had nothing to do with age as such. It was purely an effect of duration of smoking.

THE WITNESS: (cont'd.) This is interesting from the point of view of carcinogenisis, although that may not be what you are particularly interested in today.

So he suggested an experiment which my brother did, in fact. This is back to the research council in England, where they painted mice with benzopyrene, at different ages, and they confirmed this hypothesis.

In the upper graph, you can see this is the important...this is, of course, backwards...it's the proportion of mice that haven't got cancer. Mice who were first painted with benzopyrene at age ten weeks, came down like this from none of them having cancer to all of them having cancer. Mice who were painted at fifteen weeks came down exactly the same pattern, and so on and so forth.

And when you plot the same data against exposure duration, you find that the lines lie exactly on top of each other, so again you see that the cancer incidences are completely determined by time since the beginning of the carcinogenic insult, and completely unrelated to age.

This is obviously significant from a theoretical point of view, because, I mean, it has been suggested that the reason that cancer rates go up in old age is that old people are in some way more susceptible, that their immune systems are decaying in some way or another, and this is rather strong evidence that that is not the case. That it's simply the passage of time during which cellular accidents have been happening and nothing to do with age as such.

Anyway, ...

MR. LASKIN: Q. Just before you take that transparency away, can you just identify, for the record, so later we know what we are talking about...

THE WITNESS: A. That's also reference to the same paper about the age study..reference to the same paper.

MR. LASKIN: How to do...

UNIDENTIFIED SPEAKER: Tab thirteen?

MR. LASKIN: Why don't we give the transparencies all an exhibit number as...what are we up to...tab twelve, and let's call the first transparency we saw twelve A, and let's call this one twelve B, so we know what we are talking about.

EXHIBIT # 37, TAB 12 A & B: The abovementioned transparencies were then produced and marked.

MR. LASKIN: Sorry, Mr. Peto. We have to keep our public records straight.

THE WITNESS: As I say, this hasn't actually been shown directly for any human cancer. It was hypothesized as an explanation for the lung cancer data, but it couldn't be shown directly. It was shown in mice, but mice don't live very long so it wasn't a very decisive observation.

The interesting thing is that mesothelioma in asbestos workers showed exactly the same pattern.

I think this is figure one, again in the same paper, the paper that is number nine.

This is an analysis of the mesothelioma rates, cumulative risk of dying of mesothelioma, ignoring other causes of death, among North American insulation workers. This is the very large study by Irving Selikoff and his colleagues.

MR. LASKIN: Q. Just to put this in perspective, since none of us had really an opportunity to read this paper in detail, am I correct that what you have in tab nine is all of Dr. Selikoff's data from his large insulation worker study in Canada and the United States, of the seventeen thousand-odd cohort?

THE WITNESS: A. Yes.

Q. And what you are looking at is deaths from mesothelioma?

A. Yes. This is based on two hundred and

A. (cont'd.) thirty-five mesothelioma deaths. The numbers are really quite large. It's a good study.

The interesting thing about this graph is that it shows that if you look at the bottom...no, the top one first... this is mesothelioma rates...in tumors it wasn't mesothelioma... in asbestos workers first exposed at age twenty, thirty or forty, and you can see that there is a very wide separation. For the purposes of the Commission, this is a very important graph because it means that the lifelong mesothelioma risk if you were first exposed at age forty is negligible. Whereas the lifelong risk if you were first exposed at age twenty is very high.

It's really remarkable, and these are the actual data. There is no model mesothelioma. It's just straightforward data. The risk goes up to twenty percent, which is really a very high risk of dying of mesothelioma, in people first exposed around about age twenty.

Q. The first dotted line on the left is?

A. This is people first exposed at age twenty. This is first exposed at age twenty, and that's age thirty and that's age forty.

You are just dividing the cohort up in terms of age at which they joined the insulation workers union...

Q. And against that...

A. ...and the subsequent risk of mesothelioma.

Q. So can you...if you take the persons first exposed at age twenty and you draw a line across at the ten percent cummulative risk point on the Y axis, what does that tell you?

A. It tells you that by age sixty-five, ten percent of them will have died of mesothelioma.

The bottom curve is exactly the same data plotted against years since first exposure. So again, we divide the cohort up into people first exposed at age twenty, thirty

A. (cont'd.) and forty, and you are looking at the cumulative risk against years since first exposure, and the lines are identical. There is no difference whatever between...in susceptibility between old people and young people. So this is a very nice, very close analogy between ...you know, this and the mice experiment. It shows that the cancer rate is completely unrelated to age.

Q. And is really dependent upon time since first exposure.

A. Time since first exposure, and nothing else. Right.

Q. Regardless of when you are first exposed?

A. Yes. So this is a very simple...you know, it makes it much simpler to predict what this would be, expressed at various ages. It's a very simple model.

Q. Is one of the conclusions that comes from all of that that the younger...because it's only dependent on time from first exposure, nonetheless the younger you are exposed...

A. Yes, that's what the upper graph shows, that in fact the risk is ten times as high for people exposed when they are young as it is in people exposed when they are over forty.

And of course this is particularly important in relation to school children. It means when you are looking at some...if you are worried about asbestos in schools, if you start at age nought instead of age twenty, this curve would have started here, rather than here, and got up to here. So this would be, you know, of course it would be twice as high if you start an exposure at age naught rather than age twenty.

Q. Those curves are all based on Dr. Selikoff's data...

A. Yes.

Q. ...from his mesotheliomas.

A. Yes.

A. (cont'd.) Finally, in relation to that study, when you plot the two lines...perhaps I'll just obscure the bottom one for the time being, just to...I don't want to present too much at once.

This is the same data. We are ignoring age now, because we now that it is irrelevant. We are simply plotting incidence of mesothelioma mortality...

Q. You are now at figure two on the paper?

A. This is figure two of the paper, yes.

...against years since first exposure. So we are plotting time since first exposure to insulators against mesothelioma mortality, and these are logarithmic scales so a straight line means a relationship of the same sort as we've seen for lung cancer.

Q. Can you just give us an example from that figure, just to illustrate what it means?

A. Yes. The risk is one per thousand per annum, twenty-five years after first exposure. So if you had a thousand men in this cohort...

Q. Slow down again now?

A. The risk is one per thousand per annum, so if you take a thousand men twenty-five years after first exposure, in that cohort among insulators, then on average you would expect one of them to die of mesothelioma during the following year.

It goes up quite sharply. By the time you get to age fifty, it's one per hundred per annum. So that's really rather a high risk. These are incidence rates, not probability rates.

So it means if you take a cohort of a hundred men, insulators, who have been followed up for fifty years, you expect one of them to die in each successive year from that time onwards.

A. (cont'd.) So in five years you would expect five of them to die.

DR. UFFEN: Is it significant that the margin of error at the youngest age seems to be a lot greater?

THE WITNESS: Well, it's because the numbers are smaller. I mean these confidence intervals are simply based on the number of cases, and I think that's based on three cases, that there were three cases in the first group. The data are actually presented in detail in that paper, but...

DR. UFFEN: If you left that point out would it change the slope much?

THE WITNESS: No. It's irrelevant, because you won't have to...no, you can see it would be the same. It's contributing nothing to the data at all.

These don't actually matter. I mean they are not the majority of the cases. If you are calculating lifeline risks, this is the important part of the curve because that's when most of the deaths take place.

As I say, there were a total of, I think something like a review of a hundred and fifty deaths, and three of them at that point didn't have.

Q. So ten to the power of minus three on the Y axis means an incidence rate of one...

A. One per thousand per annum. One in a thousand men will die each year, at that point in the graph.

Q. And at fifty years after first exposure what does your graph show?

A. One in a hundred per annum, annual mortality will be slightly more than one percent.

As I said, the cumulative risks are shown in the previous...I mean what they mean in terms of cumulative risks of death...they mean that by the time you start at age twenty and you are followed up to age eighty, the cumulative risk

A. (cont'd.) would reach twenty percent. So there would be some magnitude of the risk, because it's quite powerful.

Q. Is there any significance to the statement at the bottom of figure two, that you looked only at those insulation workers exposed between 1922 and 1946?

A. Well, that's the difficulty with this study. The trouble is that this study was conducted in 1967 to 1976, and followed through in 1979, I believe, and so there is a complete confusion between when you were first exposed and how long you were followed up for, so these are basically data....you can regard these as being data in 1970, if you like.

So the point fifty years after first exposure is almost completely determined by people who are first exposed in 1920. Whereas the point twenty years after exposure is completely determined by people first exposed in 1950. So it isn't a proper cohort in the normal sense. There is an analysis in the paper of cohorts, and they more or less conform to this pattern, although the numbers are smaller and the period of followup not so long. Selikoff only has data from 1967 to 1979, and so there is a confusion and in the analysis in the paper it shows that the risk was actually lower in people before 1922 and after 1946...for reasons that...I assume that by 1946 conditions were improving. Before 1922 they may not have been using much asbestos in insulation. I don't know what the reasons are, but the data look as if they are fairly homogeneous from 1922 to 1946. So before and after that the risk is appreciably lower, and so if you plot the overall data, instead of getting this nice straight line you get points down here off the line, and points here off the line at the top.

Q. So you took the data that was relatively homogeneous for the purpose of this analysis?

A. This table would be actual rates with each

A. (cont'd.) year of first exposure in that paper, yes.

I think's fair, I mean it's fair both because of the internal consistency of the data and I think the theoretical consideration that you do expect cancer rates to follow this sort of pattern is a very strong one.

But I mean I think there was a lot that appeals to it among epidemiologists.

The lower line on this is perhaps logarithm, but I think it's of interest because it establishes a very close analogy between these data and the lung cancer data.

We did a survey in Los Angeles, which is described in the other paper, number eleven, and fifty-five of the people interviewed said that their mesotheliomas reported no exposure to asbestos at all. They were an interesting group, because first of all there were equal numbers of men and women, which tends to support the inference that they weren't caused by asbestos, or certainly not by industrial exposure. Otherwise one would expect more men than women.

I think there were something like eighty men who reported exposure, and about five women. Whereas among the ones who reported no exposure, and I think there were twenty-six men and twenty-nine women, virtually identical numbers. Their age distribution was quite different from the other ones. They, instead of rising as time since...the cube or the third or fourth power of the time since first exposure, like the asbestos workers... their incidence rose as the third or fourth power of age.

So this is an exact analogy between the data on lung cancer in smokers and nonsmokers, about incidence going up as a power of time since first exposure for asbestos workers, and as a power of age for those people who get mesotheliomas who aren't exposed to asbestos. The analogy between that curve and this curve for lung cancer in smokers and nonsmokers is the obvious.

Q. Can you just go back over that again for us?

A. I'll write it on the board, because they are identical, exactly the same.

Q. Can you just tell us first of all, what was your Los Angeles study?

A. We just interviewed all the mesotheliomas diagnosed in Los Angeles.

Q. In the Los Angeles area?

A. Yes. In Orange County...I think it's Orange County...the Corporation of the City of Greater Los Angeles.

Q. How many did you find?

A. A hundred and eighty-eight, and we interviewed a hundred and fifty-five of them.

Q. You tried to determine whether there was occupational exposure?

A. Yes.

Q. Just briefly summarized, what were your results?

A. I've got data on it. Do you want to...I mean, it's described in some detail in that paper.

Q. Number eleven.

A. I mean broadly speaking, the great majority of men and virtually none of the women had been exposed to asbestos.

I've shown you the data on the people who were exposed.

I mean it's an interesting study actually, because it provides estimates of asbestos exposure in the past. It actually enables you to combine these models, with the numbers of peoples who said they were first exposed at various times. You can work out what the levels of asbestos exposure were in the past and you can actually see that those low levels before the war shoot up during the war.

The most interesting thing and disturbing thing about the study is that indicates that there was no reduction after

A. (cont'd.) the war, that the fuss about wartime asbestos exposure is rather misplaced because in fact there was no improvement after the war, that in fact the conditions became bad between about 1935 and 1945 and appear to have remained at more or less that level at least until 1970. So the mesothelioma epidemic has not by any means reached its peak.

Q. Can you...you were making a distinction, at least as I understood it, between the kind of model you get in the occupational setting and the kind of model you get in the nonoccupational setting.

A. In relation to this?

Q. Yes.

A. Yes. Well, I mean the incidence of lung cancer, as I said, is age to the fourth in nonsmokers, and duration of smoking to the power of four in smokers, and the incidence of mesothelioma is proportional to age. In fact, that's about four and a half, is the best estimate.

But I mean, these exposures can't be estimated very precisely. It's in proportion to age to about the power of three and a half in the unexposed population, and is proportional to time since first exposure to asbestos...asbestos exposure to the power of three and a half, in asbestos workers.

This is independent of age. Both of these are independent of age, and this is also independent of age.

Q. Both the incidence of lung cancer in smokers and...

A. In smokers, and the incidence of mesothelioma in asbestos workers is independent of age.

Q. Okay. And both the incidence of lung cancer in nonsmokers and the incidence of mesothelioma in unexposed population is dependent on age?

A. Yes. And the inference is, as I've said, that exactly the same carcinogenic process is going on. The fact is,

A. (cont'd.) that's the same as that, and this is more or less the same as that. It suggests that the same process is happening, that the carcinogen sequence making for lung cancer and asbestos for mesothelioma just increases the background process by a very large factor.

Q. You have some...can you elaborate on what the carcinogenic process is that you think is going on?

A. I mean, I could talk all day. Well, these parallel relationships, I mean the incidence of cancer should go up as the power of time. It is predicted by the so-called multistage model of cancer, and there is quite strong evidence that cancer is caused by a sequence of changes, and I'm not saying what they are in too much detail, and that the order in which they happen is important. In fact there is a first one, and a second one and subsequent ones. But they can't just happen in any order. What they are is not known. I mean, this is the most interesting question in cancer research.

But they exist and they have to happen in a certain sequence is really rather strongly suggested both by this epidemiology and by direct experiment...I mean experiments that are done in animals where so-called initiators are given, followed by promoters, which produces very large cancer. The same two agents in the opposite order can be used - there will be no cancers. So there is very strong evidence that there are independent changes that take place when you are producing cancer, and that the order in which they happen is important.

These observations suggest very strongly that cigarette smoking and asbestos affect the first stage, because if they affected a later stage...the idea is that a first stage happens and so the number of cells involved in the first stage builds up to unite, and then the more of those there are, the larger the target population for second changes, and so on.

If you weren't affected in the first stage of

A. (cont'd.) carcinogenisis, then the risk would increase as you get older. And that's exactly what happens in radiation, of course. The older you are when you are irradiated, the higher the results of excess of cancer. This appeared not to be so because of radiation affecting a later stage of carcinogenisis, but cigarette smoking and asbestos, in relation to mesothelioma, appeared to be affecting the first stage of carcinogenisis.

Q. Is that, in my layman's terms, and in the language you just used, does that suggest that they are both, asbestos and cigarette smoking, are both initiators?

A. Well, yes, but the trouble is they are also promoters and these relationships are very different from asbestos in relation to lung cancer, and I'm going to go on to talk about that.

I mean it's really mysterious. There is very strong evidence that smoking also affects the late stage in lung cancer, and the fact that the relationships with age and time...that lung cancer in relation to asbestos...also there is very strong evidence that asbestos is affecting a late stage in the production of lung cancer and is an interaction with smoking.

This is very complicated. I mean, it seems to me rather extraordinary that the only two carcinogens which have been well studied should both affect the first stage and the later stage in different carcinogenic processes.

Q. Do you equate the first stage of this multistage process to an initiator, and a later stage to a promoter?

A. Yes. That's a synoptic and that's a good definition of initiation...I mean, is everybody...?

DR. UFFEN: Could I ask you a question, just for clarification?

Will it be important for us to understand the difference between unexposed and exposed? You had a chart on the

DR. UFFEN: (cont'd.) board a minute ago, which had the slopes of the two lines the same.

THE WITNESS: The unexposed are completely irrelevant for your purposes. I mean the unexposed people, or rather the fact that people get mesothelioma anyway, is completely irrelevant for your purposes.

And I should also say that in fact these data are very dubious. These are data as recorded by the cancer ministry, these data on unexposed people. They are as recorded by the cancer surveillance quadrant, and almost all of them have been pathologically confirmed, but they have been reviewed by the UICC, a member of the UICC panel, and quite a substantial proportion of these mesotheliomas in unexposed people have been reclassified.

So this line is really...I mean, if this relationship is true, it lends some weight to the theoretical aspects of these data...but it's irrelevant for the purposes of the Commission.

DR. UFFEN: But my question is, just for clarification, the chart in the paper we have been given only has the one line on it.

THE WITNESS: Yes. That's the only one that matters for your purposes.

DR. UFFEN: Well, we are still in a learning stage and I find it difficult sometimes to know what is important for me to understand, and what isn't. So at this stage of the game I still try to understand, and one of them is dependent on a definition of first exposure and the other one is on a definition of unexposed. They are not the same. That leads me to the perhaps naive conclusion that I really ought to understand the difference between exposed and unexposed.

THE WITNESS: Well, in this case a definition of exposed is being a member of the North American Insulation Workers Union, and the definition of unexposed is being a member

THE WITNESS: (cont'd.) of the Los Angeles population which has never been exposed to asbestos. Those are the operational definitions that these lines are based on.

MR. LASKIN: Q. I think it might help us a little, and I think there's some tables in your paper at tab nine which are of some importance. I don't know if you are coming to that, but if you are not, I think it might help us if you went through the tables and explained to us what is on them.

THE WITNESS: A. Well, I think they simply go through the data that I have shown on the graphs, more or less. The first table shows that age at first exposure is irrelevant. I mean it's an analysis which in fact, in more formal terms, shows the results of that figure that shows the age at first exposure is irrelevant to mesothelioma in asbestos workers.

Q. Okay. Can we just go through a couple of questions in detail, because just looking at table one in the paper, you there have taken all of Dr. Selikoff's mesotheliomas... that's two hundred and thirty-six...and you have divided them up between pleural and peritoneal and in accordance with the various cell categories that you've got.

Now, your expecteds, I gather, are not the kind of expecteds that we have been used to seeing in epidemiological studies which are based on external populations.

A. Yes.

Q. I notice you...this is a kind of internal expected, and I think it might help us if you told us how you calculate this internal expected and what its significance is.

A. Are you sure? Is it worth it? And I don't... I mean, the conclusion is simply what I've shown in the slide.

I'll tell you, I mean all you do is...I mean within each cohort you've got a certain number of man years, you've got people first exposed, age of first exposure, twenty, thirty, forty, and then you've got a particular time, say thirty

A. (cont'd.) years after first exposure, you've got people that have been followed up to this point in time. And you have man years of followup, so let's say that, I mean, a man you've followed...you know what that means - that someone has been followed up from the first of January one year to the first of January of the next, sort of thing...

Q. Right.

A. And let's say you have, three thousand man years in that cell, and two thousand in that cell, and one thousand in another cell. So in total you've got six thousand man years of observation.

Then...and let's say you observed a total of twelve mesotheliomas in the period thirty to thirty-five years after first exposure. So the actual rate you observed is twelve over six thousand, which is two per thousand per annum.

Then you work at the expected number in each cell by simply applying that rate to the man years. So if there's two per thousand per annum, and there's three thousand man years, the expected is six. And two per thousand per annum for two thousand years gives you an expected number of four. And two per thousand per annum for a thousand years gives you an expected number of two.

So by definition the expected numbers end up identically to the observed ones, and if you look at the bottom row, that's the case.

So then you actually look and see what the expected numbers are. If they eventually turn out to be sort of six and four and two, or more or less six and four and two, then that implies that age is not having any effect, given that your thirty years after first exposure the weight is exactly the same irrespective of how old you are.

So that's the way we would calculate it.

Q. Just one other question on table one. When

Q. (cont'd.) you talk about incidence being related to the third power of age, for example, the third power of time since first exposure, how do we do that if you take an incidence rate on table one?

A. How do you actually calculate the experiments, or how do you actually do the calculations? I mean, the ...

Q. Does that mean, for example, if the incidence rate in cell twenty-five years since first exposure is one point five?

A. Yes. In fact if you look at the next table, table two I think that is, which illustrates the point I was making about the rates actually being different in the 1922 to 1946 groups, in the early and later ones, the bottom row of that is the data, the number of cases and the number of man years for people first exposed between 1922 and 1946. Those are the rates that were plotted, in that upper line there.

The expected numbers there are calculated by fitting that model, that it's some constant time since first exposure, in fact three point two is the exponent that fits these data best, but I mean that's the...it says three point six on that slide because it was calculated before three years of update had been done. But then I think the confidence interval would have to be quite wide and I think between three and four is a better way of describing it.

Q. Does that mean you cube three point two, or you cube the time since first exposure and you will get the incidence rate?

A. Yes. I mean, for example, I mean it's actually got it at the top of the table. I mean, if you take thirty-two and a half years, for example, at a period of thirty to thirty-five years after first exposure, thirty-two and a half to the power of three point two, and you multiply that by four point four times ten to the minus eight, that gives you the weight

A. (cont'd.) for thirty to thirty-five years after first exposure, the weight per annum, and I hope that if you multiplied that number by one four seven one one, which is the number of man years, you will get forty-four point two six, which is the expected number in that bottom row. If you look in the bottom row, you have an expected number of forty-four point two six for the numbers of cases, and the correspondence between the observed and the expected numbers in that bottom row is a test of how well this model fits. And you can see that it fits very well into that.

Q. Where does the figure four point four come from?

A. It's the constant that you...I mean, that's the fitting constant, I mean the exponent. It tells you what the slope of this line is. The constant tells you where the line is.

Q. That is dependent on your data?

A. Yes.

DR. DUPRE: Counsel, could I ask a question?

MR. LASKIN: By all means.

DR. DUPRE: Mr. Peto, I'm stuck way in the back of the bus on a very, very elementary point, and my conclusion undoubtedly arises from...as an amateur trying to inject kindergarten notions of dose response into what I've been listening to.

When you point out to me that the incidence of lung cancer in smokers is proportional to duration of smoking, in elementary dose-response terms I say to myself, well, I can see how this could be, because at least the duration of smoking is one of the two elements I need in calculating what the dose has been...the number of cigarettes per time unit.

THE WITNESS: Yes.

DR. DUPRE: But then when you go to the incidence of mesothelioma among the asbestos exposed, the proportionality

DR. DUPRE: (cont'd.) is with time since first exposure, which of course does not tell me anything about the duration of exposure. It doesn't tell me either, of course, the unit of initial exposure. At this point my concept of dose starts to fall apart.

THE WITNESS: There is a very important point...there is actually a profound difference, there is one really profound difference between the data on lung cancer and the data on asbestos, is exactly that. But is in fact...I don't know if...I've got a slide, but I won't bother to dig it out...but when you stop smoking, your lung cancer rate stops going up instantly. As you stop smoking...I don't know if you have ever seen the data on smoking...the lung cancer rate goes up like that, as the fourth power of how long you have been smoking. The instant you stop, it just stops going up. It may go up very slowly, but I mean it changes dramatically, it virtually freezes, and that is not true of mesothelioma.

This is a profound difference, and the reason for this apparently is that smoking affects a late stage of carcinogenisis as well as an early one, and you stop promoting the cells. A smoker who has given up has got plenty of cells which are on their way to becoming lung cancer cells, but the last stage or last stage that one has to go through, which is also affected by smoking, drops dramatically when you stop smoking.

So this suggests that smoking affects an early stage because of these relationships, and a later stage. Whereas for mesothelioma is appears that asbestos only affects the first stage. That would be the natural interpretation of these data because the risk keeps on going up.

In fact...I don't want to go backwards and forwards between different exhibits, but if you look at exhibit ten, this thing about risk assessment of asbestos in schools, there is

THE WITNESS: (cont'd.) a table in there which deals with this.

If you look at table...where was that...yes, table one, which is on page four.

Now, if you assume that the incidence of mesothelioma which is caused by single brief exposure goes up as a cube of time... I'm not quite sure whether to write all this. Should I write on the board or what?

MR. LASKIN: You can...

THE WITNESS: I would like to leave this up because I think it's quite important. I'll do it in a corner.

DR. DUPRE: It's already written in my heart, Mr. Peto.

THE WITNESS: Well, it is very important. Underline it in your notes. It's absolutely crucial.

The mesothelioma rates go up as the sort of third or fourth power of time since first exposure. The simplest way of explaining that is that in fact if you have one fiber, if you like, one little asbestos fiber that comes in, or if you like, you are exposed for a short time, you've got sort of one year, say, or less, then you more or less got all your exposure at the same time. Then in fact the incidence that that would cause, the resulting incidence, would go up as time since then, cubed.

If you assume that every little bit of exposure is independent of all the other ones, then the bit of exposure that you got then goes under this time cubed, and if you are continuously exposed a bit and you go to the next year, it goes up as time cubed, like that. And the bit you got in the next year goes up as time cubed, and the bit you got in the next year goes up as time cubed.

So if you are continuously exposed, you add all those curves up to work out what the risk is.

THE WITNESS; (cont'd.) If you are exposed for a certain period and you stop, you add up the curves up to that point and then stop. So I mean that would be the effect, that single curve would be the effect of a year's exposure. The sum of those four curves would be the effect of four years' exposure, and the sum of twenty of those curves, I mean adding them all up, would give you a curve something like that and would be the effect of twenty years of exposure.

When you actually do the arithmetic of that, it turns out that one year of exposure, the effect of brief exposure, is to increase incidence as the cube of time, and continuous exposure will produce an incidence pattern that goes up to the fourth power of time. Intermediate exposure is given by the formula at the top of table one in...what do you call them...you don't call them exhibits, do you?

MR. LASKIN: Sure. Your tab number.

THE WITNESS: In the paper that's tab number ten, that formula, $T^4 - T - T.0^4$, which is obviously intermediate between the third and fourth power relationship, goes up in this pattern. And that table shows what the effect of different asbestos durations is.

DR. DUPRE: At what page in the tab?

THE WITNESS It's page four.

MR. LASKIN: Table one.

DR. DUPRE: Table one, page four.

THE WITNESS: That's it.

And if you look at the righthand column, the continuous at the top of that, is $T^4$.

These aren't data. The righthand column on U.S. insulators are data, but the numbers to the left are just merely calculated arithmetically. The righthand column, the continuous above it, is in fact $T^4$. The lefthand column, which has got one year, but that's duration since exposure, is $T^3$. The intermediate

THE WITNESS: (cont'd.) ones are calculated by this formula, and the thing is that they don't vary enormously. You can see that the effect of, the difference between brief exposure and continuous exposure is nor enormous. I mean they are both...

MR. LASKIN: Q. These are incidence rates that are plotted...

THE WITNESS: A. Yes. Well, they are hypothetical. They are not data. Yes. Just to illustrate what the effect of this sort of model would be, and I think it's a plausible one. Well, it is the model that I would suggest as a basis of predicting risks, in fact.

Q. Do then...

A. And so T to the three and a half, this T to the three and a half that comes out of these data, would therefore be a sort of average between the threes coming from brief exposure and the fours coming from continous exposure. The data are never good enough to distinguish the risk there, and T to the three and a half would fit either of these perfectly well because you never have large enough numbers to estimate the exponent accurately.

So this is a fairly...I think a plausible theoretical basis for predicting the effects of brief, intermediate or continuous exposure.

Q. Is the practical conclusion that taking someone out of asbestos exposure or just giving them brief exposure as opposed to longer exposure, may not greatly provide a difference in terms of his risk of getting mesothelioma?

A. No, you should look at the bottom row of that table...the bottom few rows. You will see that from one to six years, the risk is virtually proportional to duration of exposure. In fact, it's five rather than six years of exposure. The effect of one year of exposure, for example, is forty-two point five years after first exposure, the incidence is eighty there.

A. (cont'd.) In whatever units. It goes up to four hundred, so it increases by a factor of five when you have six times as much exposure. So that's virtually proportional to duration.

But if you compare to ten with continuous, there is quite a small increase. I mean, ten years exposure is almost three-quarters as bad as lifetime exposure if you were exposed from age twenty to thirty. Whether you go on working in an asbestos factory for the rest of your life or retire at that point will really have very little effect on your lifelong risk.

So I mean, it is quite important from the point of view of...I mean, you need some central model, and I think this is a plausible one, in the absence of better data.

Q. Up to about ten years, briefer exposure will make a difference?

A. Yes. Up to about...I mean, if it's up to five years, the risk will be proportional to duration. From five to ten it starts to tail off, and beyond ten it has virtually no effect. And you can see the reason for that. I mean, the reason for that is very obvious. It's that these curves go up so sharply that if you are going up as a cube of time from here, it's so high by the time you've got to ten years later that this curve never begins to catch up with that.

Q. Do you apply that model regardless of fiber type?

A. Yes. The...if you look at...

Q. Table three.

A. ...table three in the ninth paper...is it the ninth? Yes. If you look at table three in the ninth paper, there aren't data of anything like this magnitude on other cohorts. These are the only cohorts I could find where mesotheliomas have been tabulated by time since first exposure.

There is quite a variety there. I mean, there's

A. (cont'd.) the insulation workers who are exposed to practically everything, there's the Newhouse and Berry study in England, where again there was mixed exposure. There's a tiny chrysotile factory that we've studied where it was more or less all chrysotile. There's an Australian crocidolite mine where the exposure was very heavy to crocidolite, and then there's the pure amosite factory in the very brief exposure.

So in this paper you've got quite a wide range both of duration of exposure and a complete spectrum of fiber type. What this table shows, without going into the statistics in morbid detail, is that the time distribution of mesothelioma more or less fits the pattern in all these studies.

So it seems, you know, the numbers are small, but you can't say what would happen if you actually had a cohort of twenty thousand crocidolite miners and twenty thousand, you know, sort of open to study...but only given the data that are available, it seems that the time course of mesothelioma really is more or less independent of either fiber type or duration of exposure, which is an enormous simplification, of course. I mean it's very easy to sort of just apply the same model mindlessly to any form of asbestos and get more or less the right answer.

Q. I don't know whether it's the time to do it, but I did want to explore with you that point, because I note..I take the chrysotile textile factory that you refer to here is Rochdale?

A. Yes.

Q. We have heard evidence from a number of people on the question as to whether there was crocidolite at Rochdale or there wasn't crocidolite at Rochdale, and what effect, if any, if may have had. I know you are probably aware of it. There is a little footnote in the Simpson Report where it appears that they threw up their hands and said that they could never really

Q. (cont'd.) find out now what the situation really was at Rochdale, so...

A. Well, that's not entirely true, because they have been examining lung samples of people who work there. They are very late to publish the results. I mean, you would have to keep it front of you to know what the results are. I don't think you asked them. I don't know.

But the answer is that there was some crocidolite there, but not much. But the actual amount really ought to be escalated by looking at their lungs and looking at the lungs of other workers exposed at more or less the same time, who were known to be heavily exposed to crocidolite.

That experiment hasn't been done, but the only information is that there was some crocidolite processed there, but it was a very small factor in the total fiber.

Q. One of the points, I take it, that you make, from reading your papers, is that chrysotile, in your judgement, does cause mesothelioma at rates that may be comparable to cohorts where there has been crocidolite, and that the kind of mesothelioma it causes is pleural mesothelioma?

A. Yes. Yes. I mean, that's gone into in some detail in this paper. If you look at table four, in fact...table four is quite interesting because the implication of this, obviously, is that if you've got this form of the incidence of mesothelioma as proportional to time since first exposure to asbestos, to some power, then there is a constant there. It's equal to that times, some constant times that. This constant entirely determines the risk, it entirely determines the magnitude of the exposure.

What table four is, is a tabulation of what those constants actually are for different cohorts.

DR. UFFEN: Is that the one you referred to as four or about, a little while ago?

THE WITNESS: (cont'd.) a certain amount of very loose discussion of numbers in these studies. I mean, Selikoff has two hundred and thirty-five mesotheliomas in his cohort, and everybody said well, two hundred and thirty-five is a big number. Corbett McDonald only has twelve, I think, eleven or twelve among Canadian chrysotile miners, and in the Simpson Report it said, I guess there are only twelve in all those miners, the risk can't be very high.

But it's not the right denominator. I mean, you have to look at what the overall risk is in the ratio of mesothelioma to lung cancer, and in particular to adjust for the effects of time since first exposure in the way that I've done here.

When you do, you find that these cohorts at least really have very similar risks. I mean the variation is very small. I mean, the risk is actually higher in the Rochdale factory and in Newhouse and Berry's factory, as it was among insulation workers. Both of them were only of the same order.

DR. UFFEN: Could I just make sure I grasp something here in this table?

Should I interpret it in the column under the total relative risk, the one you've drawn attention to already, your own chrysotile textile factory, is only two point nine and the others are four point three. Is that difference significant? Is that what you are telling us?

THE WITNESS: No, I'm saying...it's obviously significant, yes. I was talking about the lefthand column. I was talking about the pleural mesotheliomas particularly, because there are no peritoneal mesotheliomas and I don't think anyone who has been principally exposed to chrysotile has ever had a peritoneal mesothelioma, as far as I know. Peritoneal mesothelioma seems not to occur in chrysotile workers.

It doesn't occur in crocidolite miners, but it

THE WITNESS: (cont'd.) sometimes occurs in people who work industrially with crocidolite, which seems rather ambiguous. And it accounts for the majority of mesotheliomas, fifty percent or more of mesotheliomas in people with substantial amosite exposure, so I think it's quite clear that peritoneal mesothelioma isn't caused by chrysotile.

But in terms of...the question is whether the pleural mesotheliomas in chrysotile workers are caused by chrysotile, and so for that purpose I think the lefthand column is the important one, which looks at the risks of pleural mesothelioma alone. That's the column that I was referring to, and the difference is actually quite slight.

MR. LASKIN: Q. You, in your Rochdale cohort, if I recall your figures, you have ten mesotheliomas, is that...?

THE WITNESS: A. Well, in the whole factory there have been over forty, but in the cohorts that we are actually studying, there were twelve, I think, in that analysis. It's published in the Lyon meeting.

DR. UFFEN: You just made a comment, 'the differences are quite slight'. Excuse us if it's difficult for us to grasp what is slight and what isn't.

I see for your chrysotile ones, the figure is two point nine.

THE WITNESS: Yes.

DR. UFFEN: But for Hobb's Australian crocidolite, it's five point one five.

THE WITNESS: Yes.

DR. UFFEN: Now, for those of us who are still learning the game, that's getting close to double. But you say the differences are not significant?

THE WITNESS: What I'm saying is that I think one would expect both from the limited data that are available on risk in relation to duration to exposure, and on general

THE WITNESS: (cont'd.) grounds, I mean on theoretical grounds, you would expect the dose-response to be linear.

In other words, you would expect someone who is exposed at twice the level for a given period of time, to suffer twice the risk.

Now, if crocidolite miners who were exposed under appalling, uncontrolled conditions, only have twice the risk of people who work in a chrysotile textile factory which is in fact regarded as extremely clean by the standards of the day, I mean actually it's an unusually clean factory, and within that clean factory I would think that less than one percent of the fiber was crocidolite...probably considerably less than one percent... it seems to me unlikely that you can get fifty percent of the mesothelioma rate as a result of that minute crocidolite contamination, which is the Simpson's report interpretation of the data. I think it's an optimistic interpretation. I think it's more likely to be caused by chrysotile....particularly in view of the animal experiments. I mean the animal experiments have consistently shown that at given fiber levels of a particular dimension, chrysotile is at least as dangerous, if not more so in terms of carcinogenic potential, as the other types of asbestos.

So I think that the weight of evidence, in every sense, suggests that the risk associated with the chrysotile can be, for pleural mesothelioma if not peritoneal mesothelioma, is probably of the same order as the other fiber types.

This isn't something that one can be, you know, one can be certain on. But all the weight of evidence seems to be pointing in that direction.

MR. LASKIN: Q. Do you make any difference in terms of the length of exposure or the intensity of exposure as between one fiber type or the other? And I'm thinking of the

Q. (cont'd.) gas-mask workers studies both in this country and in England. I mean, who, as I understood it, had very brief exposures to crocidolite and had a fairly high incidence of mesothelioma.

THE WITNESS: A. They also had very, very large numbers of crocidolite fibers in their lungs at autopsy. I think the data come in at the Lyon meeting, I think. There have been studies, at least in England, of the fiber content of their lungs. The mesothelioma cases almost without exception had very high fiber contents, and so they were apparently exposed to actually very high levels over a short period.

The difficulty is that I don't think there are any data in the world that relate any fiber type other than chrysotile to fiber in the lungs. There is actually nothing at all for crocidolite, and for amosite, which usually cohorts have been exposed to mixes of fibers, there are particles of fiber conversions, which are very, very dubious.

So there is no evidence whatever to suggest that the risk of two fibers per ML would be any different for chrysotile, or for crodicolite or for amosite. I mean, the data seems to be consistent with the notion that those would be...you know...I'm not saying that they are exactly the same, but there are no data to show that they aren't, as far as I know.

The animal experiments suggest rather strongly that that would be the case, and the epidemiological data are at least consistent with that.

I think we've got to the end of that.

DR. DUPRE: Mr. Peto, would you permit another very elementary question that...it follows a line of questioning that my colleague, Dr. Uffen, opened up when he asked you basically about the data definitions that were involved in the

DR. DUPRE: (cont'd.) Los Angeles study whose results are reported here, and of course are consistent with your incidence proportionality.

And the question I have is this: You get your data of mortality among insulation workers from data that is provided by the insulators union, correct?

THE WITNESS : Yes.

DR. DUPRE: That defines, of course, your exposed population?

THE WITNESS: Yes.

DR. DUPRE: Now, what you have is data that first of all shows you the number of mortalities, correct?

THE WITNESS: Yes.

DR. DUPRE: And then presumably case by case the data indicate the time of first exposure, which is probably arbitrarily defined as time of first employment?

THE WITNESS: As date of entering the union, I think.

DR. DUPRE: Entry into the union and/or initial employment?

THE WITNESS: Yes.

DR. DUPRE: Of course, there could be a difference between the two. An unorganized shop that became certified would have a disparity between time of first employment and membership in the union.

THE WITNESS: It is rather remarkable that you get this extraordinary division between curves. Those dates were allocated at random. Those curves should run into each other, and they are perfectly separated by intervals of ten years, which is what the data suggests. So I think the data are fairly reliable in that case.

DR. DUPRE: All right. Well, now, can I ask you this other question that occurs to me about your data?

DR. DUPRE: (cont'd.) The data isn't the mortalities. It gives you the time of first employment...or sorry, time of joining the union for each mortality.

Now, does it...do you also have duration of employment in the data?

THE WITNESS: No. They have certainly never tried to analyze it. I'm not very familiar with these data. I'm in a slightly awkward position. I'm pinching Professor Selikoff's data from a distance of five thousand miles, and analyzing them. They have never presented any data on duration of employment, and I understood from Herb Seidman that in fact they didn't have information on that.

DR. DUPRE: Let me tell you the reason I'm asking this question, as a layman who from time to time has to deal with numbers. Offhand my expectation would be that if you have the numbers that you have, so many deaths by so many members of a union, that of course those members of the union, whatever the number may be...let's say it's two hundred...of course, individually, to be sure, have quite different durations of employment.

THE WITNESS: Yes.

DR. DUPRE: And therefore, exposure.

But, you know, on various averages, whether you apply a median or whatever, you might well be looking at a group of two hundred which, on average, let's say had an exposure of what...fifteen or twenty years?

THE WITNESS: Yes. Yes, that's right.

DR. DUPRE: Now, I guess why that leaves me scratching my head is that is a factor there, you know, the fact that they were employed, on average, for heaven knows how long, that is not taken account of, and I guess I'm asking myself 'where does that leave me with the whole notion of time since first exposure'?

THE WITNESS: Duration of exposure and time since first exposure are two quite different things. I mean, these deaths are principally...the majority of them occur forty or fifty years after exposure. They are occurring after retirement, like most deaths.

DR. DUPRE: Well, let's say that on average there...

THE WITNESS: The question is whether or not you get a fundamentally different time distribution if the duration of exposure varies.

Now, I think that this theoretical argument which suggests that it shouldn't, taken together with the data in that table which show that different cohorts...some of which had very brief exposure indeed...conform to the same pattern.

As I said in the paper number nine, the table... three, I think, table three...which compares the distribution of deaths with the expected distribution in different cohorts, and they all more or less fit...varies between...I mean, the amosite factory, for example, that Herb Seidman studies, opened in 1941 and closed in 1945, and most of the people got less than two or three years. So these had virtually point exposures.

The insulation workers, the majority of them would have been exposed for twenty or thirty years, as you say. Many of the crocidolite miners were briefly exposed. So there is direct evidence that duration of exposure doesn't matter.

I'm not saying it doesn't matter in terms of the actual risk. I'm talking about the pattern of risk, whether or not it follows this pattern.

The question of how that is related to fiber levels is a separate one, but at the moment I'm simply saying that these relationships are clear.

So I don't think that it matters. And as I say, I mean, in fact, if you look at that table...I'll sort of go backwards and forwards between these things...but if you look

THE WITNESS: (cont'd.) at that table one that we were referring to just now, that thing about the schools, paper number ten, in fact the data on asbestos workers fit very closely the effect of ten years exposure.

I don't know how else to interpret it, but I would think you work in the union for ten years and then get promoted or retire. Or simply to the model...in fact you might note the data in the righthand column fit astonishingly closely the patterns for continuous exposure.

But that's rather just like, as I say, twenty years of exposure. I mean, coming up from ten years exposure, anyway.

MR. LASKIN: Q. So what you then did, you get the same pattern but would you then get different slopes to your curves depending on how much...what the dose was or ...

I mean, I take it there must be some difference, following up...

THE WITNESS: A. Yes, this...I mean in the extreme, you should use the cube of time, which is absolutely continuous exposure, will produce an incidence that goes up as the fourth power of time.

In fact, most of the data one has, necessarily, is somewhere between brief and fairly short. You don't actually have cohorts of people who have continuous exposure at high levels. I mean, there are absolutely none, because even the early workers...

Q. So that when you...coming back to figure one on your tab nine where you plotted your curve from year since first exposure...what power have you taken, three point five?

A. Those data aren't...this is purely the observed cumulative risk. I mean, what I've done there is, I've taken the numbers of deaths that occurred in the first sort of five year period from whatever it is..I mean, there is no model, no

A. (cont'd.) statistics in those. It would be the data.

I mean, the reason that that line goes up and then that dotted line correspondent to people age thirty-five or more at first exposure, in the bottom curve, the reason that that goes flat there is because, I think, there are a hundred and sixty man years of observation, and there were no deaths in that case. So the weight was zero. The observed weight was zero. There were no deaths at a hundred and sixty years of observation.

I mean, there's no model fitting at all involved in those curves. They are based on the whole data. It is this curve, which is a straight plot of the data restricted to 1922 to 1946 employees, and the dotted line is the...T to the power of four.

Q. Suppose, for the purposes of figure one, you just took the data, say, only those insulation workers who had worked for twenty years. Would you get a different slope to your line?

A. Those lines don't really have...the absolute level of the line might be lower, but I think that the slope would be the same.

The slope of the line...I mean, there are two separate things there. I mean, the incidence is equal to some constant times Time to the three and a half. Now, that's the slope of the curve that I was showing you. I mean that's the only line curve that used model building, and this constant depends on dose and duration.

Q. Okay.

A. What I'm suggesting is that in fact this dependence on duration is given by that pattern in that table. I think you have to assume its dependence on dose is linear. So you have three separate factors. You have this factor, which is T to the three and a half...

Q. Which determines the slope of your line.

A. Which determines the rate at which it goes up, I mean, how long it takes to double or to triple, whatever. You have this factor, the duration factor, which I would suggest is roughly linear up to about five years and then gradually tails off, and beyond ten or fifteen years it doesn't make much difference how long you are exposed for.

Then there is the dose level, which is the fibers per c.c., and I would suggest that you have to assume that that's linear, because that's the most plausible model and there are no data to support or refute it.

I mean, I think you have to assume dose linearity.

DR. UFFEN: May I clarify something right here?

MR. LASKIN: Sure.

DR. UFFEN: Is there a difference between the definition of incidence and mortality?

THE WITNESS: Not much in this case. I mean, the average survival for mesothelioma patients is in the order of a year, I think, something of that sort. I mean it isn't on there. You can find it in different data.

DR. UFFEN: Can I draw attention to something that may be a source of confusion for people? It was for me and I think I have just...in two tabs, nine and ten, similar data are presented. In tab nine, it's figure two. In tab ten, it's figure one. They are not, however, the same, and they are not entirely the same as what was on the chart.

THE WITNESS: Tab nine, figure nine? Oh, figure two. Sorry, in which one?

DR. UFFEN: Tab nine is your paper, Mesothelioma Incidence Among Asbestos Workers, and tab ten is the school one. As near as I can make it out, tab ten, figure one, has more information in it than the other one.

THE WITNESS: You mean it's got the data on the unexposed population?

DR. UFFEN: Yes.

THE WITNESS: Well, there were two differences there. The data on the unexposed population are actually in yet a third paper, number eleven. There is a table there, not a figure, but a table, table eight, which gives the age distribution in the unexposed population.

DR. UFFEN: Just to tidy things, in one case on the board you were talking about the mortality in the unexposed general population, but in your paper you crossed it out and put 'incidence'.

THE WITNESS: It is incidence. Where there were cases referred to the cancer ministry.

There are two differences. The paper based on Selikoff's data was originally based on the followup from 1967 to 1976, which is the data that has been...he has published several times and all references you have seen would be based on that followup.

Much to my annoyance, when I had written this paper he insisted on extending the followup for three years, which didn't substantially get results, but held up publication for six months.

Those data...I suppose you ought to make a note of it...these data are based on the 1967 to 1976 followup. The data in the school report, tab ten. Whereas the data that are actually finally published, you will notice the confidence intervals are slightly tighter in figure two of tab nine, and that's based on the 1967 to 1979 followup, an extra three years of followup.

The other difference in relation to the unexposed population is that the data shown in the schools report is all the cases diagnosed between 1972 and 1979 in Los Angeles.

THE WITNESS: ( cont'd.) There were fifty-five of them.

To simplify the presentation, in the paper tab eleven, in which we wrote about that, we restricted the cohort population to 1974 to 1978. So in fact...maybe I could write all that down.

So those data in the schools report never have been and never will be published in exactly that form anywhere else. In fact, since this hasn't been published, they won't be published at all.

The conclusions are poor, as you say, but that's the reason for the small discrepancy.

MR. LASKIN: Q. Could I just ask you one more question about that K constant in your equation? The K constant is the item that embodies whatever duration of employment number that you've got?

THE WITNESS: A. Yes.

Q. If you assume a linear dose-response relationship and an average dose per year, then I guess duration of employment and dose really work out to the same thing?

A. Not for longer exposures. As I say, in that table in the school report, we actually work at the constants of that formula. They work out to the same thing up to about five years, but the effect of later exposure, it becomes less and less significant simply because the incidence is determined by this high power of time since first exposure, and the fibers that you have breathed in later, within your pleura or peritoneum, have much, much less...a disproportionately reduced effect.

Q. How does dose, then, find its way into the calculation?

A. Dose is assumed, but presumably linear. I mean, this is constant as being directly proportional to the fiber level. It also depends on what size the fibers are, but I mean, I don't

A. (cont'd.) know. Presumably you've heard evidence in relation to that, but that's not a very easy question to answer.

MR. LASKIN: Do you want to take a coffee break?

DR. DUPRE: Counsel has suggested that we might pause for the usual ten minute coffee break. We'll rise then for about ten minutes.

THE INQUIRY RECESSED

- - - - - - - - - - - -

THE INQUIRY RESUMED

DR. DUPRE: Proceed, please, counsel.

MR. LASKIN: Thanks, Mr. Chairman.

MR. LASKIN: Q. Okay...

THE WITNESS: A. Am I supposed to carry on where I left off?

Q. Sure. Why don't you carry on where you left off?

A. Well, I suppose I should talk in more detail about the effects of duration and dose. I mean, this paper which deals with the risk to school children, associated with exposure from various agents...

Q. Tab ten.

A. Yes.

Q. Can you just tell us how you came to do this paper and what the purpose of it was?

A. Well, the EPA commissioned a report on asbestos in schools, which I was asked to review. It seems to me that it just grossly exaggerated the risks. I mean, it was...I don't know what's happened to it, I don't know whether it has been withdrawn or submitted, but I mean, it exaggerated the risk extraordinarily.

It took dust measurements that were taken in Paris workshops, took the highest of them, took the building

A. (cont'd.) with the highest measurements and then took the highest measurements that were taken in that building with the highest measurements, and assumed that they were typical of American schools. And then proceeded to...in fact the epidemiology, some of the errors in the epidemiology went in the opposite direction, coincidentally, but nonetheless, I mean, the final estimates were higher than they ought to have been.

So I just wrote this as sort of an outline of how I thought it ought to be done. Yes, that's its history.

And it's...I suppose in relation to what I'm saying it's quite a useful document, because it simply sets out the models that I would recommend for dose and time relationships in relation to asbestos for both mesothelioma and lung cancer.

The fact that it supposedly addresses the question of asbestos in schools is beside the point. I mean, the formulae are identical to the formulae that I think should be used in industrial control. You simply put different ages and durations and dust levels in, and you are talking about dust levels of one or two fibers rather than one or two thousandths of a fiber.

Q. Can you then...can you take us through those formulae and what you've done...slowly?

A. Well, we've already dealt with a good deal of it in relation to mesothelioma. I mean, in relation to mesothelioma if you go back to table one on page four of that report, where there is this table showing the assumed effect of different durations of exposure, the formula is that the incidence of mesothelioma, as I say, the incidence for mesothelioma is equal to some constant times the fiber level times a duration factor times Time to the three point five.

In table one, I have fitted this highly specific model which leads to estimates of the duration factor, but in the paper I just said that the effect of being exposed for continuously rather than for ten years is to double the eventual risk, more or

A. (cont'd.) less, and so the duration factor is simply adjusted in that sort of way.

You estimate this constant. The only thing you don't know there is the constant, and you estimate that constant from industrial surveys.

So, for example, I mean, the example I used in here was American insulators. I mean, it has been estimated that they were exposed to somewhere in the region of fifteen or twenty or thirty fibers per ML, for something of the order of twenty years...I mean, a cumulative dose of something like the order of perhaps three, four, five, six hundred fiber per c.c. years.

Using that sort of figure and seeing the particular incidence of mesothelioma in that cohort at the particular time gives you an estimate of K, because you know everything else.

Then I just used that constant to calculate the risks to children.

It's interesting that the risks are actually very low. I mean the risks that...there is a table, table four on page thirteen...there is a calculation of cumulative risk up to age eighty, where you are actually allowing for the fact that not everybody lives to be eighty. It turns out that something of the order of three hundred per hundred thousand people exposed from age to twelve for six years at one fiber would die of mesothelioma.

Well, the asbestos levels in the schools are usually a hundred, and...no, I think probably always a hundred, and usually very much more than a thousand times lower than one fiber per ML, so the lifelong risk would be at least a hundred, and probably more than a thousand times lower than that, which gives you a risk which is likely to be less than one in ten to the five, which seems to me negligible. I wouldn't have thought that that was worth spending as much money as you have put in.

Q. Could you just apply that formula just slowly, at least for my benefit, to the assumptions you have made to get table four?

A. Well, it's actually a bit complicated. I mean, do you want me to go through the whole of this paper?

Q. No. Tell me this, where do you get your K factor for calculating table four?

A. Well, you are trying to calculate the effect of six years exposure, which is going to be...the actual formulae that you use are that...on page seven.

Q. Page seven?

A. On page seven. It says Mesothelioma Equation Nine, and the excess annual incidence - that's the cases per year - is K times years since first exposure to the three and a half times the fiber level in the school. K...this is an estimate that is based on the data on insulation workers...is one point three times ten to the minus ten for six years exposure, or one point eight times ten to the minus ten for ten years exposure.

Q. The K builds into it the duration factor?

A. Yes. Well, the duration factor is one point three for six years, and one point eight for ten years.

DR. UFFEN: That came from the insulation workers study?

THE WITNESS: Yes, yes.

DR. UFFEN: Yours? The one that in the table called Peto's...

THE WITNESS: No, no. It's Selikoff's. It's Selikoff's data. I mean, I've written a paper about it now, but I mean they are not my data really.

DR. UFFEN: Again, why would you have used the K taken from the insulation workers, rather than from something else?

THE WITNESS: The estimates of risk don't in fact vary wildly. I mean, your estimates of risk don't vary by

THE WITNESS: (cont'd.) an order of magnitude between different studies. I mean there aren't...

DR. UFFEN: By a factor of two or three?

THE WITNESS: Yes, that sort of thing. And you presumably have already looked at the relationship between...

DR. UFFEN: Over the coffee break I tried to make an extrapolation back towards the origin for those Los Angeles unexposed workers, and I didn't take it back to age six. I took it back to age zero. I guess I got a figure of seven, instead of a figure of three or four that's in your table. Does that sound unreasonable?

THE WITNESS: I don't understand. I'm not sure what you mean.

DR. UFFEN: Okay. I guess I would interrupt things too much to try to explain.

THE WITNESS: Which graph?

DR. UFFEN: Well, the one in the schools report which has both the insulation workers on it and the Los Angeles population.

THE WITNESS: Well, you can't extrapolate back to age nought.

DR. UFFEN: Can you get a value of K corresponding to the Los Angeles workers?

THE WITNESS: Yes. I mean, that's in the table in the other paper. I mean, it's four times ten to the minus eight, and the incidence in the Los Angeles workers is...

DR. UFFEN: Yes. Now, why wouldn't you have used the Los Angeles people instead of the insulation workers when you work out an example for children?

THE WITNESS: No, no. That curve is the incidence of mesothelioma for people who were never exposed to asbestos, and that's the background incidence of mesothelioma - that lowerline. I mean, the assumption is, I mean it's

THE WITNESS: (contd.) conceivable that it's caused by ambient asbestos exposure.

I would suspect not, but I mean that's, you know, that can't be resolved and put in with the work...

DR. UFFEN: Let me put it another way, then.

You could work it out with several different examples, presumably, where you take a K from any number of different studies. Some examples are in table four that we talked about earlier.

THE WITNESS: Yes. Yes, that's right.

The thing is that most of those studies don't have dust levels associated with them. I mean, if you want to make an extrapolation of the effects of asbestos in schools, or anywhere else for that matter, you've got to be able to relate the excess mortality to measured dust level.

Now, the only one of those studies that have estimates of dust levels at all are, in fact, the American insulation workers, and that's a very dubious estimate. I mean, it was made...I mean Nicholson suddenly, about four or five years ago, said that the dust levels were ten to fifteen fibers per ML, but it was never quite clear where the estimates came from.

In fact, our factory of Rochdale, there are estimates of those, as you may know. I mean, they have been revised.

But, I mean, those are the only studies in that table where there were estimates of dust level at all.

DR. UFFEN: Would that be the reason why you would choose that?

THE WITNESS: Yes. The only possible way to proceed is to look at the excess in industrial workers where you've got measured dust levels, and then assume some model of this sort.

I mean, you know, you use them to estimate the constant in the equation, and then apply that to the effects of,

THE WITNESS: (cont'd.) you know, I mean, one fiber or half a fiber or whatever, to industrial controlling, and a hundredth of a fiber or a thousandth of a fiber if you are interested in the effects of asbestos in schools.

MR. LASKIN: Q. Your calculation of your K figure, as I take it, from what appears on page six of this paper, that's how you arrived at the K figure that you put into that equation? Is that right? Just so that I'm clear for the record.

THE WITNESS: A. Yes. That's right. That's a...yes, that's right.

Yes, their incidence of mesothelioma is three times ten to the minus three per year, thirty years after first exposure. So you just put that into the equation, and that gives you an estimate of K.

DR. UFFEN: Counsel, I hope you don't mind my trying to...

MR. LASKIN: No, not at all.

DR. UFFEN: On page three of your school study, towards the bottom of the page it explains there about the constant K, and it introduces a term 'the duration adjustment factor'.

THE WITNESS: Yes. That's the factor that comes in the table on the following page. I mean, if you assume that particular model, you find although effect obviously increases with increasing duration, it doesn't increase in proportion to the duration. So the purpose of that table is to get some idea of what it is.

DR. UFFEN: For the example to work out for the school children...

THE WITNESS: It's nought point five for six years, and nought point seven for ten years, and one for continuous exposure. I mean, that's the...

DR. UFFEN: So you use nought point five for...

THE WITNESS: For six years. It appears that six years exposure would have roughly half the lifelong risk of...something of the order of half the lifelong risk of continuous exposure.

There is also an adjustment for the fact that children don't work as long as grownups, because they don't spend eight hours a day, forty-eight weeks a year at school.

MR. LASKIN: Q. Can we go to the lung cancer...?

THE WITNESS: A. Yes.

I don't know. I mean, is everybody reasonably happy this far? I mean, I can't obviously sort of take it all in detail immediately, but I think what I have done is spelled it out in some detail in these various things that have been distributed today.

For lung cancer, the effect seems to be...is very different. Remember this formula for lung cancer...I'm going to do asbestos as the effect of lung cancer incidence in nonsmokers and lung cancer incidence in smokers. Although that is analogous to the mesothelioma pattern produced by asbestos, the effect of asbestos in relation to lung cancer and smoking seems to be quite different.

Roughly speaking, whatever your lung cancer rate would be for the nonsmoker...this is your lung cancer rate, if you are smoking this is your lung cancer rate...it seems that asbestos simply multiplies it. So in fact you can write down the formula very simply. I mean, the formula for lung cancer rates in people exposed to asbestos is simply exactly the same formula with one plus an asbestos effect. So if there was no asbestos effect, there would just be one. That would give you the ordinary rate when people aren't exposed to asbestos.

What's more, it seems to be the same whether you are a smoker or a nonsmoker. This is the relative risk for that. So you have exactly the same incidence of lung cancer for

A. (cont'd.) people exposed to asbestos. It seems to be exactly the same as for people who aren't exposed to asbestos, at a particular age, so on and so forth, simply multiplied by a constant.

So, I mean, that's just another way of saying that the relative risk for lung cancer...the relative risk is just equal to one plus some constant times the cumulative dose. So this is a much easier formula than...it's much easier than the mesothelioma situation because cumulative dose is just duration times level of exposure. All you do is estimate K, one plus some constant, times duration, times average dust level.

Now, this is a model which has really been...I think it's fairly generally accepted now, and there are actually quite a lot of data to support it.

The sort of patterns of relative risk that you see in asbestos workers are these, and these are relative risks... this is in fact the amosite factory that Seidman and Selikoff studied, and it's an interesting example because the exposure was intense and brief, and the relative risk shot up really quite quickly, and then stayed at the same level. It's interesting, it's generally believed that the relative risk goes up slowly when people are exposed to asbestos, for lung cancer, and I'm not sure that that's true.

I think the reason it goes up slowly may be because most people are exposed to relatively low levels over long periods, and in fact in this case, certainly, where the exposure was heavy and brief, the relative risk was really quite high early on.

The data on the insulators...

MR. LASKIN: Can we just record that slide, for the record, as slide number...

THE WITNESS: Well, I don't know whether you want to... you've got that paper by Bill Nicholson, the paper that went to Helsinki, but that's taken from that, that's one of the figures in his paper.

MR. LASKIN: All right. We do have that paper.

THE WITNESS: But it's one of the figures in his paper, and so is this, in fact. This is also one that appears in his paper. This is the relative risk for lung cancer in the insulation workers.

Now, this doesn't follow such a beautiful pattern, but I think that the reason it doesn't follow such a nice pattern is first of all because they were exposed not as intensely for a long time, and so this period when the relative risk was going up was also a period when they were accumulating dose.

So according to this formula, if the relative risk just goes up...stops at one and then just goes up in proportion to cumulative dose, you would expect a straight line starting at one, as long as you go on exposure. It's going up like that.

So I think the fact that it increases in this way, while in a group continuously exposed, is what you would expect according to that formula.

The fact that it falls at the end is difficult to interpret, because these were so extraordinary and this was a population where they got a relative risk of six for lung cancer and a very high incidence of mesothelioma, a very high death rate from asbestosis, which would kill both the people most heavily exposed within the cohort...there's obviously some heterogeneity...and the smokers. So I think you would actually expect to see an eventual fall in the relative risk. So I don't think you can claim that this formula is well enough established to found profound scientific theories on it. I think perhaps it's a reasonable summary of the available data, that in fact if the dose were lower then you weren't actually wiping out all the heavily exposed people and the smokers.

But you would have seen a pattern which went more like that, and then stayed more or less constant. So that's the basis of this assumption.

THE WITNESS: (cont'd.) The other basis, of course, is the direct plots of...sorry, this is lung cancer in asbestos workers, at the top of the slide...these are plots of cumulative dose against relative risk for lung cancer, which I expect you've seen before.

These are actually figures taken from that paper that I wrote in the last of 1978. I've just put here that at that time nobody believed that the dose response was linear. It seems to be more generally accepted now.

When these data were originally published, both Enterline and McDonald said that because there wasn't a significant excess there, there was the same threshold in terms of fibers, in terms of million particle per cubic foot years, they both did say that to me.

So there seems to be a fairly good straight line relationship between relative risk starting at one and going up, and cumulative dose.

So, I mean, all these data are consistent with this sort of fairly simple notion.

So it seems a reasonable basis for calculation.

Curiously, nobody has ever, until that paper, until that recent paper by Bill Nicholson, nobody has ever looked in detail at what actually happened to people exposed at different ages. They support it as well. These are Selikoff's data again, and as you look at the ratio of observed to expected for lung cancer in smokers...ignore the nonsmokers for the time being...in smokers...then in fact the people first exposed at age twenty, the relative risk is about six.

For people exposed first at age thirty, it averages about six. For people first exposed at age forty, is an average of about four. But, I mean, it certainly isn't changing grossly with age at first exposure, and the assumption that it is more or less constant seems a reasonable approximation.

THE WITNESS: (cont'd.) This makes another interesting point, which is in relation to what happens to nonsmokers.

The expected numbers in this table are calculated as smoking specific, so these are expected numbers of lung cancers among smokers. The data for nonsmokers give expected numbers of lung cancers among nonsmokers, and the numbers are too small to look in detail at different ages, but you can see there is no evidence of a change.

The overall relative risk is six, exactly the same as the risk for smokers, so the effect of exposure seems to be...the relative risk seems to be independent of age and independent of smoking. The risk is therefore ten or twenty times bigger in smokers, because their lung cancer rate is ten or twenty times bigger.

It's quite interesting to put these lists together with what I was saying before about mesothelioma, because the risk for mesothelioma starts going up from the time of first exposure. The risk is enormous if you were exposed when you were young and very small if you were exposed when you were old. These are the actual numbers of cases, without any model fitting here. These are the actual number of cases in this cohort of lung cancer and mesothelioma for smokers and nonsmokers first exposed at different ages.

It's quite interesting compared to what the ratios are. There is an excess here of two or three lung cancers, and fifteen mesotheliomas, in people exposed...nonsmokers exposed when they are young, and they will be the workers of the future, one hopes. In this cell, there are more or less six times as many mesotheliomas as excess lung cancers, so mesothelioma is by far the most important cause of death in people who don't smoke and who are exposed when they are young.

In this cell, where you are exposed when you are

THE WITNESS: (cont'd.) exposed when you are old, and you are a smoker, there is an excess of about forty-five mesotheliomas...forty-five lung cancers, rather...to eleven mesotheliomas.

So the ratio of excess lung cancer to mesothelioma varies as you change from smokers to nonsmokers and go from people exposed when they are young to people exposed when they were old, from six mesotheliomas to one lung cancer here, and to four lung cancers to one mesothelioma there. So there is a factor of twenty-five and a very different pattern.

Here lung cancer is the main problem, and here the major problem is mesothelioma. So you can see how...I mean this is rather direct evidence that these models are important, and you have to take this into account when you are deciding to legislate for them.

Of course, extrapolating this backwards for children, you will see in that schools thing that in fact the children who smoke, who go on to smoke, I mean, the risk for lung cancer and mesothelioma are more or less the same. For children who don't smoke, the lung cancer risk is completely negligible because of the mesothelioma risk.

So this is sort of direct evidence, you know, I mean supports these models really rather precisely.

Yes, I mean Selikoff's data are going to show the same thing. These are more or less what I've already shown. These are people first exposed at different ages, sort of twenty, thirty, forty, and these are lung cancer rates. This is restricted to smokers now, so they are not identical to that graph I showed you before. That's the cumulative risk of lung cancer plotted against years since first exposure to asbestos, and you see the extraordinary difference. Because the lung cancer rate is high in people aged sixty, which is twenty years after first exposure to asbestos, people who were

THE WITNESS: (cont'd.) aged forty at first exposure, so age sixty at this point on the graph, their lung cancer rate is already high, and the asbestos exposure multiplies it, so they have a very large risk fairly soon.

Whereas the people who are younger at first exposure, all so young at a given point on this graph, have much lower lung cancer risks.

So you get very big differences thirty years after first exposure, in the lung cancer risk, and people who were exposed when they were young rather than old.

Nonsmokers have a negligible risk, which goes back to smoking, asbestos multiplied.

For mesothelioma, there is no difference whatever between people exposed...people at different ages at first exposure...or between smokers and nonsmokers.

So again, those are data, the actual data is quite straightforward.

DR. DUPRE: Where do the last two slides come from?

THE WITNESS: These are not published. In fact, I've put them in a dirty brown envelope in...

MR. LASKIN: I think what I'll do is...

THE WITNESS: I can continue on and show you Selikoff's signature on those.

MR. LASKIN: What I will do is arrange to have them photocopied after, and distributed. I think that's the easiest thing, and I think we'll be able to work out what Mr. Peto was referring to there, rather than interrupt him.

THE WITNESS: I think this is a very interesting slide. It makes the point...again, it's all very well with these models...but to make the point directly, that is a ratio of six-to-one and one-to-six in the actual crude numbers. It's quite interesting.

DR. MUSTARD: Can I ask a question? Just leave that on.

THE WITNESS: Yes.

DR. MUSTARD: Could you explain to me why...I guess we are dealing with different numbers of people in those two groups, the smokers and nonsmokers? That is the observed mesotheliomas at fifteen in the nonsmokers and ninety-nine in the smokers? You didn't look...

THE WITNESS: We looked at three or four, probably four times as many smokers as nonsmokers.

DR. MUSTARD: I just want to make it...that's the explanation for it, because all the other ones we've had is that smoking does not influence mesotheliomas.

THE WITNESS: It didn't in these data.

DR. MUSTARD: Okay. It's just the cohort size?

THE WITNESS: Yes.

It may be of some interest to mention that in fact this is a graph of lung cancer rates in sort of young, middleaged people, against cigarette smoking, in 1950. It is generally believed that lung cancer rates are much lower in both America and Canada than they are in Britain, and the thing about this graph is that it shows that this in fact isn't the case. It is true of older people, but then your cigarette consumption was much lower than ours before the war. Since the war you have caught up with us, and in fact in America, at least, you have now overtaken us.

If you put the graph of lung cancer rates at age forty in 1975, you get a cigarette consumption per capita in 1950, you find that America now has the highest lung cancer rates in the world, and the highest cigarette consumption in the world, and this was in 1950, and the rates are still going up rapidly in older people.

There is England, and there is Canada, more or less

THE WITNESS: (cont'd.) next to it. So I mean, the projections in these various things, I mean sometimes these English rates, and sometimes the American rates, and so on and so forth, but I mean, it may not be true now, but it will in the future be true that something of the order of ten percent of Canadians and Americans will die of lung cancer, as is presently true of British men.

I don't know if this is worth mentioning particularly, but there is a certain confusion because incidence rates and prevalence and cumulative risk and lifelong risk, and so on and so forth, and I don't know whether I ought to just explain what is going on.

In the case of mesothelioma, if you take the example of people born in 1900, and first exposed to asbestos at age twenty in 1920, or at age forty in 1940, or at age sixty in 1960, someone first exposed at the age of twenty has an incidence that goes up as time since 1920 to the three and a half, so I mean that line would go up something like that, and his incidence curve would go up like that, and that would be time since 1920 to the power of three and a half. That would be the incidence curve for mesothelioma.

Now, not everybody lives forever, and this is a survival...an average American born in 1900. So to work out how many mesothelioma deaths you are actually going to get, you multiply that incidence curve by the probability of survival.

So in fact the risk is extremely high by the time you get to age eighty. Your chance of being there is drastically reduced, and so the actual numbers of cases occurring at age eighty, in that group, would be lower than the number of cases occurring at age seventy.

The total risk is the area under that curve, the total risk of mesothelioma when you were first exposed at age twenty.

THE WITNESS: (cont'd.) If you were first exposed at age forty, you have exactly the same incidence curve. The incidence curve is identical, but you are immediately multiplying it by a very quickly falling survival curve, and so the actual numbers of cases and therefore the risk, which is the incidence under that curve, again is much lower. If you were first exposed at age sixty, then the risk is negligible because you would die before you had time to get the disease. You would die of something else first.

So in one of the tables there is a calculation of lifelong risk. Lifelong risk is the area underneath these curves, and of course from a legislative point of view it's the most important thing. That is actually what matters. It's not the fact that the cumulative risks in the mesothelioma paper are independent of age - it's neither here nor there.

I mean, the lifelong risk is negligible if you are exposed when you are old, and this calculation of multiplying incidence rates by survival curves is what it's based on. I think it's quite important that in fact predictions should be based on lifelong risks in that way, because that's obviously what is important. So that's purely academic interest, the effect of mesothelioma is the same at age of sixty as it is at age twenty.

On the relation of different kinds of fiber, it has been said that there are gross differences between different studies in the mesothelioma incidence, and as I said earlier, it was pointed out in the English report that said that only eleven mesotheliomas out of eleven thousand Canadian chrysotile miners was possibly very high.

On this slide is a comparison between numbers of mesotheliomas and the excess of lung cancer. These are observed and expected numbers of lung and pleural mesotheliomas together.

The ratio, in fact, doesn't vary very much in different studies. In the Canadian chrysotile miners, for example,

THE WITNESS: (cont'd.) which are the basis of the assertion...the only basis, I think, for the assertion that chrysotile doesn't cause mesothelioma...the ratio was eleven out of a total excess of forty-six, so they constituted twenty-four percent of the excess of respiratory cancer.

In Herb Seidman's amosite factory, I mean, one of the, you know, best established of the agents that cause mesothelioma is sixteen per hundred - seventeen percent was the ratio - slightly lower, in fact, than in the chrysotile mines.

In insulation workers, it was a hundred and seventy-five mesotheliomas out of an excess of four hundred and thirty. So they constituted forty-one percent of the excess.

But in fact, only sixty-three of those are pleural, so if you look at the incidence of pleural mesothelioma, which is in fact what these figures are about, to the excess lung cancer, that figure would be about twenty percent, and it would be slightly lower than the excess in the chrysotile mines.

The crocidolite mine is an interesting example. This was cited in a paper that McDonald...which you may have seen...a paper which McDonald presented at the recent meeting in Coldspring Harbour, when he said that there was a far larger excess of mesothelioma than of lung cancer.

In fact, in the paper that was originally presented to the Lyon meeting, there was a division of that cohort into migrant and nonmigrant workers. The migrant workers had completely ridiculous results. They had no excess of lung cancer and gross deficiencies in deaths from all other causes, and a very large number of mesotheliomas.

What it seems is happening is that first of all the followup was poor, and secondly, the mesotheliomas were being picked up anecdotally and clinically, and included in the paper.

If you confine the analysis for the sort of normal Caucasian population who were properly followed up, that

THE WITNESS: (cont'd.) study falls absolutely in line with all the others, with nine mesotheliomas out of a total excess of respiratory cancer of twenty-seven, giving thirty-three percent being due to mesothelioma.

So the idea that there are gross differences between different fiber types in their carcinogenic effect really doesn't seem to be supported by the data.

There is one exception to this, and I don't know how to explain it. It's a paper by Rossiter in the Lyon meeting, where there was no excess of lung cancer at all, and thirty-one mesotheliomas. I suspect that the same thing may have happened and in fact mesotheliomas were identified anecdotally. But I don't know.

But as far as I know, that's the only exception.

MR. LASKIN: Q. What about the paper by Dement?

THE WITNESS: A. Well, yes.

Q. I understand it only has one mesothelioma.

A. Well, of course, I don't know what the total excess of lung cancer is. What is the excess of lung cancer in that paper? Has anybody got the data there?

There is a total excess of eighteen.

First of all, this obviously varies to some extent with duration of followup. I mean, when you look at the graphs I just showed, particularly older workers, you get quite a sharp increase in the excess of lung cancer. Whereas the mesothelioma risk doesn't begin to go up for slightly longer. So if you had a rather short followup, this ratio doesn't...I mean, I've already pointed out that the ratio of lung cancer to mesothelioma can vary from six-to-one to one-to-six. So it isn't...I'm not certain that this is a sufficient way of doing the calculation, saying that there is a sort of crude rule of thumb. It really indicates very little difference between the two cohorts.

THE WITNESS: (cont'd.) I mean, let's suppose that twenty percent of them were supposed to be mesotheliomas. You would expect something of the order of four. So if you've got one, and you expected four, it really isn't a particularly staggering exception.

Because the paper by Rossiter was a gross exception. There were thirty-one mesotheliomas and apparently no excess for lung cancer at all, and I suspect that there must be some artifactual reason for that.

I think this is an important point. I don't know if anybody has any particular questions in relation to it, but I mean...I think there are some well known facts about asbestos which are simply sort of taken as false and are really not supported by any decent evidence at all. This is one of them.

This is a very simple basis for calculation. I mean, if you assume that the relative risk for lung cancer is equal to one plus some constant times duration times average dust level, then any cohort in which you have observed a substantial relative risk, in which you estimate this constant, then you can simply apply the same calculation to other groups.

It implies that age at first exposure makes no difference whatever to the risk, because if this relationship is true, then the normal lung cancer risk, the normal incidence of lung cancer, whether you are a smoker or a nonsmoker, goes up sharply with age in that sort of way. The relationship may not be exactly the same, but you get this sort of pattern of increasing risk.

Let's suppose that you've doubled it. Let's suppose that this multiplies together to one, so the overall relative risk is two. You've got one plus one, you've calculated the risk.

Then the effect of asbestos exposure...say you were first exposed at age twenty or forty or sixty, the great

THE WITNESS: (cont'd.) majority of lung cancer deaths occur after age fifty, and I think more than half of them occur after age sixty. So even if you are exposed first quite late in life, if the effect of asbestos exposure is to bump this curve up in that sort of way, and then to run on at double that level, then your risk will be doubled throughout the part of your life when all the lung cancers occur, and so the difference between being first exposed at age forty, which would produce this factor of risk rather than this...this is the risk in an unexposed person... unexposed smoker or nonsmoker...as I say, the effect is the same, that the risk is doubled. I mean, the nonsmokers' risk may be low, you draw the same graph with a different vertical axis, but the pattern is the same.

The effect of asbestos exposure at age forty is to double the risk in that sort of pattern. If you were first exposed at age twenty, you double it in this sort of pattern, so the only difference between being first exposed at age twenty or forty, or nought for that matter, is this tiny little bit here, which is negligible.

So for practical purposes, you can calculate what the lifelong risk of lung cancer associated with a particular exposure is, by simply seeing what proportion of the population die of lung cancer. If you double the relative risk, that's the proportion that are caused by asbestos, and if you have a cohort in which the relative risk is two, as ten percent of Englishmen die of lung cancer, then the relative risk of two for lung cancer among asbestos workers means that ten percent of those asbestos workers get killed by it. If half a percent of nonsmokers die of lung cancer, the relative risk of two means that a half a percent of asbestos workers who don't smoke will be killed by it.

MR. LASKIN: Q. Does latency have any affect on all this?

THE WITNESS: A. Latency is...I mean, latency is a completely sterile concept. It doesn't really arise, and the incidence pattern follows these relationships, and obviously because they tend to go up sharply with time, most of the deaths occur late.

But latency is a completely unhelpful concept. I mean, there is no such thing really. I mean, there's obviously two or three years between the existence of the cancer and its diagnosis, but that's not normally what is meant by latency.

The reason you don't see mesotheliomas within five years of first exposure is because the risk is so low within five years after first exposure. If you exposed a million people to massive doses of asbestos, I'm sure you would do.

DR. UFFEN: Does your comment also apply to quite low exposures in schools, for example?

THE WITNESS: Oh, yes. I mean, I think that both from the data that you have and theoretically, you would expect these...

DR. UFFEN: For the slow-witted among us, like me, would you just go through this for three ages - an elementary school child, a secondary school student and a university student where the ages are twenty-off?

THE WITNESS: Well, for lung cancer it makes no difference, because I mean, you...I must say, actually, the thing about lung cancer is that there aren't any data on people who were exposed to asbestos before they started to smoke. So it's conceivable that the effect of exposure when you were young is very much higher.

I mean, if you've got a lung cancer process which starts when smoking starts, and you know that asbestos initiates the mesothelioma process, it's conceivable that it initiates the lung cancer process and that in fact this would be proportionately higher in people exposed as children.

THE WITNESS: (cont'd.) Yes, I mean I can't really comment on that. I mean, I doubt if it's true, but I mean I don't...there really aren't any data that have been able to answer the question.

DR.UFFEN: We've been pushing it too hard to try to start making that kind of calculation then?

THE WITNESS: No. What sort of calculation? I mean with this model, the calculation is simply that that's what the lung cancer rate would have been if you were exposed when you were forty. It goes like that. If you were exposed when you were twenty, it goes like that. If you were exposed when you were nought, it's undetectable anyway at that stage, and so you will simply follow this up the curve at a given level of exposure. So...I mean for a given total dose it is completely irrelevant what age you were first exposed at. You simply seem to be just multiplying the normal incidence pattern by this factor, and if you are exposed for twice as long, the increase in risk would be twice as high. If you are exposed to twice the dose, the increase in risk would be twice as high. But the actual pattern would be exactly the same, and that's why latency is such nonsense. Because the age distribution is the same.

This pattern determines the average age at whch you die, unless the risk becomes so high that nobody survives to old age. As long as you are talking about relatively low doses, the average age of death from lung cancer in nonsmokers, for example, is lower than in smokers, and the average age of death from lung cancer in asbestos workers who smoke tends to be older than in nonasbestos workers. The effect of exposure in fact is to increase latency, rather than to reduce it.

So I've explained that. It's worth explaining because it's something that is very...it really isn't understood, but it seems sort of intuitively obvious that you'll get

THE WITNESS: (cont'd.) something earlier if the risk is greater, which isn't the case, in fact, at all.

For a start, the data on lung cancer in smokers and nonsmokers, it's immediately obvious from the graph that I showed earlier. I mean, the risk goes up as the fourth power of age in nonsmokers, and more steeply in smokers. So the relative risk for smoking is about four when you are thirty. This is nonsmokers - nonsmokers and smokers - this is lung cancer observed, and this is incidence.

The risk goes up increasingly steeply if you are a smoker, as you get older. So it's obvious that the weight of deaths would occur in old age rather than in youth, with the average age of death of smokers from lung cancer would actually be older than the average of death of nonsmokers from lung cancer.

This was true directly in our study in Los Angeles...in fact, I've got the data here somewhere...in the actual age distribution of the unexposed mesotheliomas for exactly the same reason, because they follow the same pattern.

The young ones are predominantly unexposed. I mean, I think there were no asbestos workers who got mesotheliomas before the age of forty or forty-five, whereas there were one or two unexposed people.

If the effect of asbestos exposure is to increase this yet again...so you are going up because you are a smoker, and then you were exposed to asbestos at age thirty or forty... then your lung cancer curve is going to be bumped up again, and this will weight the curve towards older ages. So the average age at which these deaths occur, these deaths in smoking asbestos workers, will be slightly higher than the average age at which these deaths occur in smokers who aren't exposed to asbestos, which will in turn be higher than the average age at which they had lung cancer deaths in nonsmokers occur. So the effect of...as you add exposure, the effect is to actually increase

THE WITNESS: (cont'd.) the latency, to increase the average age of death.

So the idea that you should do a correlation of the sort that Liddell did in the Lyon meeting, between the time from first exposure to death from lung cancer, and expect it to be correlated with dose, is ridiculous. I mean, it's a question which is...and latency, as I say, in fact has no meaning and tends to go not in the direction of the way that most people think.

DR. UFFEN: I may have missed it, on your graph you plotted lung cancer incidence against...you don't label it there.

THE WITNESS: Sorry.

DR. UFFEN: It's gone now.

THE WITNESS: I'll draw it again, but I mean really it is misunderstood this, and I mean it's misunderstood by some statisticians, actually.

I suppose probably the easiest way is to actually sort of write numbers down. I mean, let's suppose...just to simplify things...you say you've got nonsmokers, you've got smokers without asbestos exposure, and you've got smoking asbestos workers. Let's take sort of age groups in the forty to forty-nine, and fifty to fifty-nine, and sixty to sixty-nine, and seventy to seventy-nine, and let's suppose you've got a thousand of each.

Now, let's suppose that the incidence here is going to go up to the fourth power of age, so I don't want to get into a lot of complicated arithmetic, what I'm basically saying is, let's suppose that there is one death there and three there, and sort of five there and seven there, lung cancer deaths among these thousand nonsmokers.

Now, in smokers you know that it's going to go up more steeply. The relative risk of smoking increases as you get older. I mean, it's about...it's of the order of eight at age

THE WITNESS: (cont'd.) forty, and it's of the order of ten, so there would be about thirty there, and sort of the order of fifteen, I suppose. We'll have to have more than a thousand people, because we'll run out of people to die in a minute.

At the order of fifteen at that sort of age range, and it gets to be twenty or more here. Perhaps we had better make it ten thousand people.

If you were exposed to asbestos around about the age of thirty, say, then your relative risk of lung cancer won't go up initially...particularly if you were exposed continuously. Then it would go up a bit by the time you are here...the relative risk is one here...and then let's say it's one point five by the time you get to here, and then by the time you get to this range it has doubled - a hundred and fifty and then two hundred and eighty.

Then it is immediately clear that the average of these numbers is going to be lower than the average of these numbers, which is going to be lower than the average of these numbers, the ages at which the deaths occur.

Is it okay? I mean, eventually you will get a situation where the exposure is so high that it actually kills people off, and then you'll start to actually lose the deaths at the top end, and then of course you will actually get a reduction in latency, so you have two competing effects, neither of which you have particular interest in.

I mean, it's an unhelpful concept and it's completely...it isn't worth analyzing. The proper way to look at all these things is in terms of incidence rates which are, I mean, easy. I mean, they are independent of each other in successive areas, and they've got some scientific meaning.

I don't want to do it now, but if you actually do compute the average ages of deaths there, you will find that they

THE WITNESS: (cont'd.) are actually higher here, than here and here. So the...

MR. LASKIN: Q. Because of the multiplier effect?

THE WITNESS: A. Sorry?

Q. Because of the multiplier effect?

A. It's because the relative risk increases with age in both cases, so the preponderance of deaths occur in old age... the preponderance of excess deaths particularly.

So that...I don't know what the numbers actually are...but perhaps you are going to have the average age of death something of the order of sort of sixty here, the average age of death.

It doesn't change enormously, but I mean something of the order of perhaps sixty here, and perhaps about sixty-five here, and perhaps seventy here. That sort of thing.

But most people would prefer to have sixteen lung cancer deaths with an average age of sixty, than five hundred with an average age of seventy.

Is that okay? I mean, it isn't...it isn't okay?

DR. UFFEN: Your last comment depends on whether you are sixty or seventy.

DR. DUPRE: I just want to ask you this, Mr. Peto, one thing that I have been taught should always be borne in mind when one is looking at any epidemiological study is that it takes no account whatsoever of age at death. You know, ten deaths at age seventy or ten deaths at age fifty, basically simply show up respectively as ten deaths in a lot of studies.

Now, ...

THE WITNESS: In fact it happens that the age of death is almost always the same, whatever happens. I mean, whatever you are doing - whether you expose children to asbestos and look at the mesotheliomas, or wether you smoke, or whether you smoke and you are exposed to asbestos, or whatever, or you

THE WITNESS: (cont'd.) call it heart disease. I mean, the age distribution of most deaths, and of most excess deaths, is really very much the same as the age distribution of all deaths.

I mean, broadly speaking, a death that's caused by anything, there is an average age of around about sixty-five. You evaluate its consequences on that basis, and I think that there is...yes, there is a table in fact, table four in the schools thing...illustrates the point. Table four and table five.

If you look at the column in table four which... one, two, three, the fourth column across in table four in the schools paper...computes expected number of deaths due to mesothelioma, within an approximate multiple, obviously...the fourth column, third from the left...is deaths in different five year age intervals among children exposed to asbestos from the age of twelve, and the vast majority are occurring after the age of sixty.

So, although...I mean, I am not suggesting it's a good thing to expose children to asbestos, but you shouldn't be emotional about it. I mean, the age distribution of the deaths that are caused by it will be the same as the age distribution of the deaths among industrial workers exposed to asbestos. And the same is true of lung cancer. In table five, two pages on, you've got the same thing.

The distribution is deaths due to lung cancer, caused by early exposures, and is likely to be very much the same as the age distribution of deaths from lung cancer anyway.

In fact, it's true. There are differences...

DR. UFFEN: It's not very different from the mesothelioma. Table four and five are about the same.

THE WITNESS: They are very much same, yes.

DR. UFFEN: I'm trying to remember what I had

DR. UFFEN: (cont'd.) for breakfast now.

What does that, the suggestion that it's the mesothelioma that is the problem with very young school children?

THE WITNESS: I'm talking about the distribution of deaths by age. I'm just saying the majority of them have occurred at the age of sixty. The absolute level of risk...

DR. UFFEN: Yes, not the absolute value, sorry.

THE WITNESS: The absolute level of risk will be very much higher if you were exposed when you were younger.

It isn't absolutely true. I mean, I'm not saying there is no variation. I mean there is a variation with age at first exposure, and so on, but basically when you look at any curve which goes up as a power of time or age, the vast majority of deaths occur in old age and it makes no difference what the power of time is.

I mean, if you have an incidence going up as a cube of time, or the fourth power of time, or the seventh power of time, then the weight of the curve will always be on the righthand side, and the vast majority of deaths will occur after the age of sixty, irrespective of what the exposure is or when it occurred.

MR. LASKIN: Q. I think I understand what you have been talking about here, but the latency concept that we have been used to talking about is relevant in terms of your analysis of mesothelioma in that mesothelioma is related to time from first exposure, which is a kind of latency concept.

THE WITNESS: A. It isn't a latency concept. The only definition of latency is a period in which nothing happens.

Q. All right. Maybe that's the problem.

A. Or the risk is going up increasingly fast, and so the majority of deaths occur late. But, I mean, there is no latency. It's a completely sterile concept, and it isn't...

A. (cont'd.) I mean, there is a paper...if I can find it, there is a magnificent paper in the Lyon meeting about mesothelioma among children.

I don't think I can find it, but it says that the most spectacular difference between mesotheliomas among children and those among adults is the extraordinarily short latent period in children.

Can you spot the silliness in that statement? I mean, it's rather difficult to have a long latent period to get a mesothelioma when you are a child.

DR. MUSTARD: I take it that...I have two comments.

MR. LASKIN: Go ahead.

DR. MUSTARD: I take it you are using your anti-latency comment, it's the true epidemiological, biological scientists' concept that events start occurring when you recognize them, clinicians may say it took me ten years before I could recognize it, and things like that. That is one place where you get trapped in the concept of latency.

But I think the distinction you are making is a scientific, mathematical analysis approach to the problem, versus the standard clinician's attitude that asbestosis doesn't exist until I can recognize it clinically in my huffing-puffing machine.

THE WITNESS: There is a latency to diagnose asbestosis quite clearly. But true, I was talking particularly about cancer incidence. I mean, there is actually a latency of the order of five or ten years in any method of...

DR. MUSTARD: In the diagnosis of asbestosis.

THE WITNESS: Yes, that's true.

DR. MUSTARD: Yes, but I would challenge you, if I may, that the same events are going on in the lung related to asbestosis, as cancer, and so if you had the skills of measuring

DR. MUSTARD: (cont'd.) what was going on at the actual pulmonary site, probably the definition of latency would have the same kind of problem that you are having with the cancer definition.

THE WITNESS: Yes. Yes.

DR. MUSTARD: Let me go to your table, your mesothelioma and your lung cancer tables, and the important thing in the heading, for those of us worried about what we have to do as a Commission, is exposure at one fiber per ML.

Now, it's that magic word 'one fiber per ML' that's in your calculations. That one fiber per ML is based upon the fiber concept in the Selikoff study, I presume. Is that correct?

THE WITNESS: Yes.

DR. MUSTARD: So whatever that fiber value means is what that fiber means, and I think you have said that their fiber classification was kind of arbitrary.

THE WITNESS: Yes, yes.

DR. MUSTARD: So we have an interesting puzzle that that figure there is powerfully determined, I would presume, by whatever the definition of fibers happens to be.

I was wondering if you had any neat solutions as to how to get around a definition of fiber.

THE WITNESS: Do you want the K's in all the formulae? It's the most important question, isn't it.

DR. MUSTARD: Let's suppose that fiber value is out by a factor of one hundred.

THE WITNESS: Then you are able to underestimate the risk by a factor of one hundred.

DR. MUSTARD: Well, in either direction. What happens to...can you quickly tell me what the magnitude of the change is in that calculation?

THE WITNESS: Yes, exactly. I mean, you'll either

THE WITNESS: (cont'd.) increase or reduce the risk by a factor of a hundred, and that's the trouble.

MR. LASKIN: Shall we stop for lunch?

DR. DUPRE: We'll close for lunch. Shall we break until two-thirty?

MR. LASKIN: Sure.

THE INQUIRY RECESSED

- - - - - - - - - - - - -

THE INQUIRY RESUMED

DR. DUPRE: Are you ready to proceed?

MR. LASKIN: I sure am. Thanks, Mr. Chairman.

DR. DUPRE: Proceed, please.

MR. LASKIN: Mr. Peto, could I just ask you about one or two final questions about that chart which you put up just before lunch, which I understand shows, because the increasing relative risk, that smokers who are exposed to asbestos in fact will have an average age at death which is higher than nonsmokers or smokers who aren't exposed to asbestos.

THE WITNESS: A. Yes.

Q. Is it also true though that smokers exposed to asbestos will have a greater loss of expected life than they would otherwise have had?

In other words, they will...

A. Yes, yes.

Q. ...have a shorter life expectancy than your nonsmokers or your smokers not exposed to asbestos?

A. Yes.

Q. Can we, from the tables that you presented, is there a way to calculate what the loss of life expectancy is because of the interaction of smoking and asbestos, or just asbestos?

A. The loss of expected life is almost always

A. (cont'd.) about fifteen years. For any cancer and for most diseases which are caused by practically anything, I mean in general, the death rates, normal death rates, I mean the normal death rates for most cancers and for heart disease and for respiratory disease, and the cancers that are caused by asbestos or the cancers that are caused by smoking, or the excess of heart disease that is caused by smoking, has more or less the same age distribution as the death rate for all causes in the general population.

That isn't exactly true, but it's roughly true. I mean, heart disease deaths are slightly earlier, lung cancer deaths are about average among men who have smoked all their lives. Deaths from chronic bronchitis in smokers tend to be slightly later. But broadly speaking, they have more or less the same age distribution, so if you calculate life expectancy and average it over the distribution of deaths that are caused by any of these things, the loss of expected life is nearly always about twelve or fifteen years.

So roughly speaking, you can compute the loss of expected life by working out what proportion of people die as the result of the exposure, and multiplying it by fifteen years.

A third of cigarette smokers are killed by smoking, and the ones who are killed lose fifteen years each, so the average loss of expected life caused by smoking is five years, which is a third of fifteen.

As a rule of thumb, that gives you a very good idea. I mean, it's never less than ten and never more than twenty.

So as a rule of thumb..I mean it's obviously not true of childhood leukemia, but broadly speaking it would be true of most of the asbestos-related diseases.

I suppose it wouldn't be true of asbestosis deaths

A. (cont'd.) in people who were exposed very heavily when they were young, but I mean that's not...I mean, that sort of extremely heavy exposure doesn't occur anymore.

So it would be roughly true for asbestosis as well, under relatively low exposure conditions.

Q. Unless you were going to say anything more about what you were talking about this morning, I was going to move to a different subject.

A. Sure. I could just say in relation to that I suppose it is helpful to see this in perspective. I mean, if you talk about one percent lifelong risk under certain conditions...I mean what that actually means in terms of loss of expected life is one percent of fifteen years, which is something of the order of two months.

I think that's right. I mean, the loss of expected life, if you kill one percent of the population, the loss of expected life of the average asbestos worker, who suffers a one percent excess risk, is two months. Although I am not suggesting that this is an acceptable risk. I mean, I think you ought to see it in perspective. It is not in the same order in which people have suffered in the past.

Q. What you are saying is, if you, for example, posit a certain standard for asbestos and the basis of that standard is that it will cause an excess risk of one percent, over a given lifetime, at a given dose...

A. I don't know what...I'm sorry. What did you say?

Q. Let me start again.

Take the approach that the British took in 1968, which was to base a standard on, I guess, the fact that one percent of what standard would yield one percent of persons developing a morbidity index.

A. Yes.

Q. And if you translate that to mortality and plot it against loss of expectancy of life, is what you are suggesting that the average loss of expectancy will be about two months, by rule of thumb?

Or have I got it wrong.

A. It's one month, isn't it? Fifteen years is a hundred and eighty months. Yes, it would be about two months. Right.

Q. Okay.

What does that mean for any particular individual? I guess that's really what I'm trying to get at. Particular individuals exposed, let's take a hypothetical example, particular individuals exposed to whatever dose you may name, and that dose hypothetically will mean that he has, let's say a one percent excess risk of dying of an asbestos-related disease - lung cancer.

What does that mean in terms of his loss of life expectancy?

A. You mean if one percent of people are killed by lung cancer as a result of their asbestos exposure?

Q. Yes.

A. As I say, it means a loss of expected life of the order of two months, but whether that means that one percent of the population will lose fifteen years, or all of them lose two months, is a pretty ambiguous question. I'm not sure how much it matters.

I mean, the trouble is, with mesothelioma, of course, you can identify the individuals who are killed, and they have lost fifteen years each.

But in relation to smoking, for example, it's quite clear that smokers who get lung cancer wouldn't have got it if they hadn't smoked, and those individuals have lost fifteen years each.

A. (cont'd.) Smokers who die of heart disease, it is not at all clear that that doesn't happen to susceptible individuals, and those people may...were certainly at higher risk than average, and you could even say that they have actually had a fairly short amount knocked off their life because those people who died were actually destined to die of heart disease.

Destined is the wrong word, but were at much higher than average risk of dying of heart disease, and that those particular individuals had been selected and had their lives systematically shortened.

So, there is a spectrum from individuals such as those who get mesothelioma who have quite clearly been chosen, quite probably haphazardly, by the exposure and killed fifteen years early, to a situation where you have got people who are susceptible, perhaps to heart disease, and have had their lives systematically shortened by a small amount.

So it's a question which is...it's a curious question. I'm not sure that there is a meaningful answer to it.

It's a scientific question, and in a way it's a biological question which, the answer to which isn't really known. It's different for different diseases.

Q. Fair enough.

Can I turn...what I was going to turn to was your own work at Rochdale, and ask you some questions about that, and then alternately try to put your work at Rochdale in the context of your comments on the Simpson report, the Advisory Committee report.

Can we start, just to put the study at Rochdale in context, and the work in Great Britain in context, I think it would help this Commission here if you could just tell us generally the regulatory framework over the years against which we should be looking at the Rochdale study.

By that I mean, can you tell us generally the

Q. (cont'd.) kinds of asbestos control standards there have been in Great Britain over the years, and in particular pre-1931, and then what change there was in 1931, and working its way upwards?

A. Well, I'm not an expert on this. I mean, the 1931 regulations said that no dust should be allowed to escape. They were more stringent than the current regulations.

But the form that they took was just specifying in detail what technical improvements should take place; that certain forms of ventilation were mandatory in certain circumstances; that certain work practices were to be forbidden, and so on.

I mean, they were the result of the work by Merewether, who recorded extraordinarily high incidents of asbestosis in heavily exposed men.

Q. There was no numerical dust count limit?

A. Not at that time. In fact, I'm not sure, and perhaps somebody else probably knows, but I think that a specific dust or particle count was introduced at sometime between then and the two fiber standard which was introduced in 1969 or 1970, but I'm not sure about that.

I don't know if anybody else here knows the answer, out of the audience.

So I'm not certain of that point. I mean, the two fiber standard was introduced in 1969 or 1970, as a result of the...

Q. Yes.

A. ...which was the incidence of crepitations.

Q. But looking at your own comments through your papers, on what happened in 1931, first of all, I take it that there is some consensus that that regulation achieved some measurable lowering of whatever dust was in the asbestos workplace at that time?

A. Oh, yes. It had an enormous effect. It was generally accepted.

I mean, some factories are very much better than others at enforcing it, but I mean it certainly had an enormous influence.

I mean, Rochdale is a good example. There's a factory where the excess risk was colossal in people who had been heavily exposed before that time, and is very significantly reduced after...in people who started working after that time.

DR. DUPRE: That nature of that 1931 regulation was, as I heard you put it, that no dust should be allowed to escape?

THE WITNESS: Yes. And it was obviously...

DR. DUPRE: From what, to the plant to the outside environment, or from the operation...?

THE WITNESS: I'm really not an expert on this, but as I understand it, I mean the legal requirement was that certain things should be done. As I said, that certain ventilation should take place, that certain practices should cease.

But I think the terms were that no dust should escape, should be allowed to escape, but it obviously wasn't enforced. I mean, it meant that the huge visible clouds that had been normal in the past should be done away with.

MR. LASKIN: Q. And then...I appreciate from some of your comments in the papers, that as I understand it there were no measurements of any kind at Rochdale before 1951. Is that correct?

THE WITNESS: A. There may have been sporadic measurements, but there was no systematic program of measurement.

Q. I note in one of your papers you make the comment that dust levels started to come down from about 1945

Q. (cont'd.) onwards, and I'm wondering was there something that happened in 1945, was it just the end of the war, was there some even that caused dust levels to start to come down?

A. It was completely anecdotal. I mean, there was never good evidence that there had been a substantial change. It was even conceivable that after the considerable cleanups which took place in the thirties that people thought the problem had been solved, and conditions got worse again.

I really wouldn't like to say what the pattern of dust levels was between 1931 and 1950, at Rochdale.

I mean, the mortality data, which I think are probably the best measure of...better measure of what conditions were like than anything else, indicate that if anything, conditions were worse after 1954. But I mean, you know, I just don't know.

Q. You discuss it in a number of places, but one of the places in which you do discuss it is in your paper at tab one, at page 172. Perhaps I take it, just from looking at the last part of page 171 that perhaps the answer is really contained in there, and you make the point that the dust regulations may have been relaxed during the Second World War.

A. Yes. I mean, the things that are said about dust rules there, and measurements, come from the company, and I'm really not competent to comment on them. The measurements were taken routinely from 1951 onwards, at first with a thermal precipitator, then with membrane filter from 1961 onwards.

Q. When you say routinely, how often would routinely be?

A. I'm not sure. They were taken quite frequently in quite a large number of areas, but I don't know the details.

Q. More than once annually, I take it?

A. Yes, that's my understanding. But as I say,

A. (cont'd.) I really don't know about it in detail.

I assume this must have been gone into in the original BOHS study, because these are the same measurements that the current hygiene standard is based upon, of course. I mean, this factory has a peculiar significance in that it was in fact the factory on which the current two fiber standard was based. I mean, the analysis based on these data. This is the only formal justification that has ever been offered for the two fiber standard.

Q. In 1968, the standard was based on...

A. Yes, on these measurements.

Q. At Rochdale.

Can you...is there any judgement amongst the people with which you were associated when you wrote the paper at tab one as to the reliability of the thermal precipitator as opposed to...we appear to use over here...which is the midget impinger?

A. I was told that it was very much more reliable.

Q. Which was?

A. The thermal precipitator was very much more reliable. It was producing measurements which were quite comparable and more or less linearly related to membrane filter counts. But I don't know whether or not...I don't know how true that is.

I mean, the correlation between the 1960 measurements in particular areas with a thermal precipitator, and the 1961 measurements with membrane filters, in fact comparing the two columns in table five on that page...although not perfect, is better than the correspondence between the particle counts and the fiber counts which were taken by actual parallel measurements in the Quebec mines.

A. (cont'd.) These aren't parallel measurements. Parallel measurements were in fact taken at Rochdale, and they were used as the basis of the conversion, but I have never seen the data. I mean those conversions were done by people within the factory, and conversion factors were worked out. My understanding is that the correspondence was actually quite good when parallel measurements were taken.

Q. Between the thermal precipitator and the membrane filter?

A. Yes. But as I say, I mean, simply looking at the two columns in this table, you can see...

Q. What table are you looking at?

A. Table five, on page 172 of tab one. The correspondence between those figures, although not magnificent, is actually better than the virtually zero correlation that was found when parallel measurements were taken in Quebec mines between particle...between the impinger counts and fiber counts.

As I say, there is a good deal of variability here because these are measurements taken a year apart in the same area, whereas the Quebec comparison was based on parallel measurements.

So I think it would be fair to say that these measurements from 1951 to 1960 are the very much better estimate, provide a very much better estimate of what fiber counts would have been over that period than anything else that is available, even if they are not perfect.

Q. When you make that judgement and you say than anything else that was available...I'm sorry, Dr. Uffen, I' ll get to you in one moment...are you making a judgement of the reliability of measurement at Rochdale as compared to your view as to the reliability of the measurement in other cohort studies?

A. Yes. I don't think there is any other cohort

A. (cont'd.) study which has reasonably reliable estimates in terms of fibers, over this period. I think this is the only cohort study in which there were moderately good measurements over a period when people were...where you can see sort of measureable morbidity and excess mortality among people who were first employed at the time when the measurements were taken.

DR. UFFEN: Do you happen to know whether the thermal precipitator method has any influence on the size or aspect ratio of the dust from the time it is taken in to what it measures?

THE WITNESS: I don't know. I'm sorry, I don't know.

DR. UFFEN: Do you know how it works?

THE WITNESS: Not in detail, no. I'm really not an expert on that.

MR. LASKIN: Q. Just pursuing this a bit further, the calculation to work backwards in time to get the fiber counts, can you just briefly take us through it? As I understand it, there has been two steps. You go back, you do some ratio calculations back to 1951, and then pre-1951 you add on a factor?

THE WITNESS: A. In a sense, I think the data before 1951 are rather irrelevant now, because there are substantial data on morbidity in people who started working in 1951 or later, and significant excess of lung cancer. I'm not sure what the value of the earlier data is anymore, because there are no measurements during that period. The assumptions that were made before seem inconsistent with the epidemiological data.

I mean, to assume that the dust level was actually higher during a period when the excess of lung cancer was lower, seems anomalous.

Q. The cohort that you are now principally looking at are those employed from 1951, onwards?

A. Yes.

Q. To get from 1969/70, backwards to 1951, can you just tell the Commission how that was done, just briefly?

A. From 1969...?

Q. When were the first membrane filter counts?

A. 1961.

Q. 1961, I'm sorry. To get from 1961, backwards to 1951?

A. Parallel measurements were taken during that period, and conversion factors were calculated, and that was done by the hygiene offices in the factory. These estimates, these tables of estimates, were provided by them.

Q. In other words, you had a precipitator count, as I understand it, for 1960, as against a membrane filter count for 1961?

A. Yes.

Q. And you took that ratio and applied that ratio to prior thermal precipitator counts?

A. Yes.

Q. To get your fiber counts.

Now, I just want to follow in time a bit the changes in the estimates which you have taken into account, and what are in part referred to in the Simpson report and indeed, in part, Mr. Berry spoke to us about.

As I understand it, the 1968 standard was based on data that measured area sampling as opposed to personal sampling, and whole field view rather than graticule?

A. Yes. Yes, that's right.

Q. Mr. Berry, when he was here and gave evidence, and indeed he suggests in one of his papers, I think, that even taking those figures into account, the dust estimates actually

Q. (cont'd.) were about two-thirds of what the British report in 1968 said they were.

I, just to start with, wonder if you had any view on that.

A. Sir, could you say that again?

Q. I better, so I won't misquote him...and you may be familiar...I take it the group out of Wales, which includes Mr. Berry, they have been looking at morbidity in the Rochdale plant, and your group, and you in particular, you have been looking at mortality?

A. Yes.

Q. There is a paper which he presented to us, which you may be familiar with, which is his paper in the British Journal of Industrial Medicine, 1979, called Asbestosis - A Study of Dose-Response Relationships in an Asbestos Textile Factory.

A. Yes.

Q. He makes one...one of the points he makes, which is at page 105, is that he says the dust exposures are now known more accurately than they were in 1968, and in particular it is known that some men spent part of their time in less dusty jobs than the job category defined in 1966, and the effect of this extra information is the average cummulative dose up to 1966 is now estimated at about two-thirds of what it previously was thought to be.

A. Yes.

Q. Does that accord with your understanding of the situation?

A. The same data, I mean the data that I was given, were in fact his data. Geoff Berry, in fact, supplied these estimates in tab one, on page 172. They were actually the data that the...the BOHS committee was reconvened in the early 1970's, and at that time the original, 1966 data, were revised, and he was given individual estimates. The cohort

A. (cont'd.) that he studied, morbidity was, in fact, almost the same as the cohort that our mortality study was based on.

So he actually used those estimates, the BOHS estimates, which he used in that paper, and computed, for example... I mean the reason that the average actually goes up from 1936, I think to 1941 in that table, is because it is weighted by the number of men exposed in each area, and it happened that there were slightly more men in slightly dustier areas in 1941. It wasn't that the individual estimates varied greatly. It was a shift of the distribution of workers, and so on.

So those figures in the 1977 paper, that tab one, are the same as the data, estimates, which he is using in the British Journal of Industrial Medicine in 197...

Q. 1979.

A. 1979. And in fact the same results are summarized in a paper by him in the New York Academy of Sciences, in 1979.

Q. Now, can I then take you from that point to your revision of the data which appears at tab seven of your booklet, and that's your 1980 paper at...

A. Yes.

Q. If we go to page 832, table two, which sets out your revisions.

A. Yes.

Q. First of all, how did it come about that these revisions or recalculations were made? Is this something that was done by the company internally?

A. Yes. I mean, the BOHS committee was reconstituted in the early seventies, and the dust estimates were revised. I mean, there were new estimates which, as you say, were slightly lower than the estimates that had been used in ...they were lower? Surely they were higher.

A. (cont'd.) Did you say they were two-thirds lower?

Q. Two-thirds....? That's what Mr. Berry would suggest, as I...

A. Sorry, could you read that section?

I thought they were revised upwards.

The data were revised for the reconvened BOHS committee, and then that committee sat for some time, and the medical physics people in the factory became increasingly unhappy about the estimates and decided they were going to revise them again, in fact. The proceedings in that committee were suspended, and in fact it never reported. They didn't submit a report to the Simpson Commission. I mean, the intention of the committee was to submit a report to the Simpson Commission, and in fact they never did so because of the dust estimates, in fact. They became unhappy about the dust estimates and suspended the proceedings and set about a revision.

This was supposed...the committee was supposed to reconvene with the new estimates, but nothing ever came out of it. I mean, I don't know what happened after that.

The estimates that I put in my 1980 paper, at tab seven, are in fact the estimates which have been revised again, so there have been two revisions of the original 1966 data, the 1968 report, which the current standard is based on.

There was the revision of those which led to the analysis that Geoff Berry published in the British Journal of Industrial Medicine in 1979, and in volume 330 of the New York Academy of Sciences. That was 1979.

Then there was a further revision, which, as I say, has never seen the light of day as a formal analysis, but I was given the individual measures on certain individuals

A. (cont'd.) in this cohort, to work out average levels, and that's what's reproduced in that table.

Q. Okay. Does that reflect a revision that takes account both of the change from area to personal sampling, and the change from full view to graticule? Or just one of those factors?

A. It's...supposedly it only takes account of the change to graticule sampling.

Q. I guess I asked that question because your revisions seem to be different than the revisions that appeared in the Simpson Report, and in, as I understand it, that revision formed part of its quantitative risk assessment, which is the reason I'm trying to take you through this.

A. I'm in a very difficult position in relation to this, because as you can gather from what I've said, I mean I've basically been given rows of numbers twice, and published them. I'm really not in a position to comment on how the revision was done, or why the changes were quite as great as they were.

Q. Do you have any judgement one way or the other on the recalculation that was done in the Simpson Report, which as I understand it was to...let's see if I can...that as I understand it...perhaps I should put this in front of you, but looking at table thirty-seven in the Simpson Report...and I take it they relied on Mr. Steel's recalculations, the industrial hygienist. They seem to give a factor of two point five to the graticule change, and two to the personal sampling change, to come out with a conversion of five.

A. Yes.

Q. Do you have any judgement one way or the other on that conversion, in light of your own recalculations?

A. I don't know. Not really, except that it is

A. (cont'd.) the most important question facing the committee. I mean, there are plenty of studies that have got...

Q. Exactly.

A. ...you know, excess mortality and significant morbidity, and no association with dust measurements.

When you see apparent discrepancies between different studies, and conversions have been done from one measurement technique to another, and then you find that within a study which was supposed to be the definitive one that dust measurements have now been multiplied by a factor of five, despite the fact that they did actually correspond to membrane filter measurements taken by modern technique, you have to...I mean it is very important, you should understand what the basis of those conversions is and to decide whether or not they are valid.

Because a factor of five is being introduced, which effectively increases the hygiene standard by a factor of five, and there is now publicly available evidence from which to judge its validity.

Q. Is that still the situation today?

A. Well, in the sense that there is no public evidence available to judge its validity, yes. But I mean, I don't know what to say. You know, it is a curious situation.

Q. Can you, in trying to assess this can you help us any further in trying to assess the conversion factors that were used in the Simpson Report?

A. No. I mean, that's their basis. Their basis is a factor of two point five for the graticule, and two for the personal sampling. I mean, in another point in the Simpson Report it says that the effect of, the results of personal sampling were in fact more or less the same as static sampling at low dust levels. So it isn't clear that a factor

A. (cont'd.) as high as two should be used.

Q. Just take that one slowly again?

A. In the article by Steel, in volume two of the Simpson Report, it says that the ratio of personal to static sampling is variable, but in areas of good dust control the ratio is close to one-to-one.

So it isn't clear what level you should use a factor of two.

Q. I see.

The two point five for the full view to graticule, I take it, is somewhat akin to your revisions in the 1980 paper? I mean, that seems to be roughly the kind of factor you were working with.

A. I think that's because they applied that factor to calculate the numbers, so it may not be a coincidence.

Q. I see.

DR. UFFEN: Could I ask a question here, counsel?

MR. LASKIN: Sure.

DR. UFFEN: In the review paper that you had called, The Establishment of the Industrial Hygiene Standards - an Example, what's your...I'm not sure what tab number this is. I haven't got a number.

On page 110 of that, there is a figure one that shows ...

DR. DUPRE: Tab three.

DR. UFFEN: Is it tab three?

It shows dust levels in fiber per c.c. for 1920 to 1972. First of all, I'm not sure whether it's the same...

DR. DUPRE: Excuse me, Dr. Uffen, I made a mistake. It is not tab three, it is...

M. CASGRAIN: Two.

DR. UFFEN: Is it two?

DR. DUPRE: Two.

MR. LASKIN: I'm sorry. What page are we at?

M. CASGRAIN: Page 110.

DR. UFFEN: Page 110, and I just happened to notice that in that rough chart the ratio is five-to-one for the period from 1920 to 1933, and then from 1933 to after 1950.

THE WITNESS: That's a sheer invention. I mean, that is simply a schematic illustration. The fact that the dust level was assumed to be very much higher...in fact, that probably isn't a true pattern. There were considerable improvements during the twenties. I think the dust levels were...

DR. UFFEN: It's just an accident that it was used to...it goes from fifty to ten, which is a five-to-one...

THE WITNESS: Oh, yes. Imean, that's just to illustrate the fact that nobody knows what conditions were like, but they were certainly worse before 1930. I mean, there obviously wasn't an astonishing improvement in the six month period in 1933. What actually happened is that there was a very considerable improvement during the twenties, and by the time the regulations were introduced in that factory, at least, most of the improvements had already taken place.

But from 1933 owards, those are simply the data that are reproduced in the 1977 paper, and again, of course, they are guessed from 1933 to 1950.

MR. LASKIN: Q. Can I just ask you, in view of the comments you just made about the importance of these conversion factors, the dust estimates and so on, that in view of the discrepancy that one, for example, sees between what you have written and what Mr. Steel has done, do you still stand by the judgement you made about the reliability of the Rochdale data as compared to the data in any other cohort study?

THE WITNESS: A. It seems to me that since the...oh, yes, I would do, yes. Because I don't think that... the processes of the conversions that have taken place here are at least well documented...but it seems to me that the

A. (cont'd.) appropriate solution in this case would be to impose static sampling restrictions, that since you've actually got static samples, you've got fairly good estimates of what the static sample measurements would be if you use whole field counting rather than graticule counting, and it seems to me that a fairly straightforward way of solving the problem is to have the pattern of static samples which are monitored by the government, and are counted in the same way as they were from 1961 onwards, in England, and you then have direct comparability, and whether or not this factor of five is valid will be bypassed. You could, at the same time, investigate whether it is valid, but to presuppose that it's valid when there is very considerable doubt about it and it may make quite a bit of difference to the risk, seems to me unsatisfactory and I would have thought it would have been reasonable to impose restrictions on the basis of the techniques that were actually applied at that time, because there is a series of vicious circles there. I mean, there are technical changes which introduce such a measure of uncertainty in the extrapolation from one period to the next in each case, that it's never possible to impose restrictions with any degree of confidence.

Since a method which was in fact measuring the particles which are still being counted, albeit by different technique, since those measurements on the basis of these relationships, I mean that would seem to me a sensible way around the problem, since there really is a lot of uncertainty and the factor could be anywhere from one to more than five.

Q. I want to take you to your two mortality studies in a moment. Perhaps this is a good time to deal with one of the comments that you made to me in the original letter you wrote to me, which is at the beginning of your tab number three.

If you turn to...I think it should be there...

Q. (cot'd.) But you had, what you indicated was your two major disagreements with the Simpson Committee Report, and I wonder if we could...we have dealt with the second one to some extent, and perhaps we'll come back to it, but can we first of all deal with the first one?

A. Yes. I mean, I think that...

Q. Would it be of assistance to you if I give you a copy of the report?

A. No, that's okay.

The point really is that the estimates of risk which are presented in the Simpson Report on the basis of different studies, actually are inconsistent. When you have inconsistent estimates of risk, it isn't good enough to average them. You have to explain the inconsistency.

In particular, when you are dealing with something of this sort, you have to explain why the highest ones are as high as they are. Because if you choose a risk estimate which is lower than the highest ones, then you are explicitly assuming that those high estimates of risk are wrong, and you need fairly strong evidence for that.

Now, it's quite clear that the estimates in relation to chrysotile mining in Canada are extraordinarily low.

Q. Can we just...so that we all know what we are talking about...are we now talking about the Simpson Report or the Acheson study, table thirty-five, where it takes...

A. Yes, in which the...

Q. ..the three studies - Quebec, Enterline and your study...

A. Yes, and various multiplying factors were applied both for converting particles per cubic foot to fibers per ML, and for allowing for graticule on the counting in personal sampling.

Q. This is the risk assessment you are talking about?

A. Yes.

Q. Okay.

A. Now, the estimates, the range of estimates that come out of that are from...is a range of more than tenfold, in fact...in the risk at a specific level of exposure.

Those are inconsistent and it seems to me that the studies which produced the highest risk estimates ought to be looked at and either accepted or criticized, but should be... it should be possible to say why the results are so grossly wrong.

The Rochdale results produce rather high risk estimates, and Rochdale was chosen as the basis of the BOHS study in 1968, which as I say was the basis for the two fiber standard in England, and I think in Canada and the United States in most of Europe, because the dust measurements there were regarded as being the best available because dust measurements had in fact been taken systematically over a long period, and because morbidity, and now mortality, had been studied in that factory.

So to ignore the risk estimates that come from that factory, particularly since it is an industrial setting, which I would have thought was more relevant to at least the English experience than chrysotile mining, although you may be more interested in chrysotile mining here...

Q. We don't have any mining here either.

A. ...seems to me illogical.

I mean, I think a coherent rationale for doing so ought to be offered, and I feel that wasn't done in this report, that in fact these inconsistent estimates were presented and one more or less in the middle was chosen rather haphazardly. And that in fact a more formal consideration, particularly of the Rochdale data, should have been offered.

You see, the conversion factors which are used

A. (cont'd.) for converting from particles to fibers, in this table, are really based on extraordinarily inadequate data.

I don't know if you have ever seen the graph, which I think...I'm not sure if it's in here...the graph of the parallel measurements in Quebec, of fibers and particles, which was published in 1974. I've got a slide of it, if I can find it, and it's pretty spectacular. It looks like a shotgun from a distance of twenty yards, and the correlation is absolutely zero.

Q. Perhaps if you had the slide and it's handy, it would be helpful to us to see it.

I take it you are going to show us...is this the attempts by Messrs. Gibbs and Lachance to convert?

A. Yes. Yes, this is a correlation. This is a graph of the results of parallel measurements. These are adjacent measurements with a midget impinger and a membrane filter, and today's rather strong influence is on the number of fibers that have got to produce a particular level of risk, on the basis of the conversion which is depicted here.

It seems to me slightly dubious. They are virtually uncorrelated. You get a point here...

Q. Could you just explain to us...

A. ...where there is an estimate of more than thirty million particles per cubic foot at a fiber count somewhere in the region of five fibers per ML, and another situation here where there is a measurement which seems to be less than one million particles per cubic foot corresponding to a fiber count of a hundred fibers per ML.

These are the data that are being used, in effect, when a conversion from particles to fibers is produced and used for analyzing the Quebec data, and it seems to be completely worthless. I mean, I don't think that it's...I think it would be reasonable in the mines to say that even among the

A. (cont'd.) people who are very heavily exposed for a long time, the excesses weren't colossal, and to apply engineering improvement properly based on particle counting, and I think that's in fact what was done.

That would seem reasonable in the mines, but these data to me seem to be completely irrelevant for control in industry.

Q. Those data are irrelevant, is that what you said?

A. Well, you can't use data of that quality to convert particles to fibers. It's clearly absurd.

DR. UFFEN: If it were to be a reliable one, you would expect to see them all clustered at least along some curve going up to a center somewhere?

THE WITNESS: Yes. I mean, they are completely rounded, as you can see.

DR. DUPRE: Do we have that, or may we have that slide?

MR. LASKIN: We will certainly obtain a copy of that slide.

DR. DUPRE: As part of our record.

THE WITNESS: Do you want the article? It is reference, I think, in...I've got a copy of the article with me, actually, if you want to take a copy of it.

MR. LASKIN: Perhaps that would be helpful. I think it's actually in our compendium of articles for Dr. Gibbs, but we had better make certain of that, and I'll check that at the recess.

THE WITNESS: Yes, there it is.

MR. LASKIN: The article, just to read it into the record, it is in the compendium of Dr. Gibbs' publications, but it's Dust Fiber Relationships in the Quebec Chrysotile Industry, and it's found in the archives as Environmental Health,

MR. LASKIN: (cont'd.) February, 1974.

MR. LASKIN: Q. Apart from your comments about the conversions, is another thing you are saying that a mining cohort ought not to have been included in a risk assessment where you are trying to regulate in an industrial setting?

THE WITNESS: A. No. If the results are consistent, then it would add weight to the data. But the results are so grossly inconsistent, and there is a very obvious explanation for their inconsistency, there virtually is no conversion that is of any use whatever for converting particles in a mining context, to fibers.

That makes them irrelevant. I mean, the results in relation to those conversions, and the basis of the conversions, not that it's mining as such.

I mean, there may very well be big differences between the textile situation and the asbestos cement situation as well.

Q. Do you have any judgement on the use of the Enterline cohort study for the purpose of this risk assessment?

A. Well, I think the same criticism is true, that the actual basis of the exposure estimates is weak in that study as well.

Q. If you were doing the risk assessments yourself, would you have simply taken the Rochdale study and looked at it, or would you have included any other cohort studies, yourself?

A. I don't know what other studies exist, for which measurements have been taken. I mean, obviously it would be of enormous value to have other cohorts in which fiber counts, or something which could be reasonably converted into fiber counts, were available.

Q. When you say...when you wrote to me that you believed there had been a substantial underestimation of the lung

Q. (cont'd.) cancer risk, can you quantify that more particularly?

A. Well, when the Simpson Committee met, in fact, we hadn't reanalyzed the Rochdale data. We hadn't analyzed and published the results of the followup on people first exposed up to 1950.

Q. Is this your 1980 paper?

A. Yes. That hadn't been published at that time.

But the results of that extension of the followup are rather disturbing, because this is the first good data on the population, as I say, where the dust levels were actually measured. The earlier papers were based on the estimates of dust levels before 1950, whereas from 1951 onwards, they were measured. So there is a reasonable basis for conversion.

Q. What is disturbing about them?

A. Simply the magnitude of the risk at a relatively low dust level.

I mean if you look at the...

Q. Why don't we look at that for a moment.

A. I don't know which...

Q. Is it in your...I take it that it's in your tab seven, your updated mortality study?

A. Yes, that's right.

Q. Is it table one at page 830?

A. Yes, table one.

The relative risk for lung cancer in the bottom half of the table, which refers to people first employed in 1951 or later, shows eight lung cancer deaths compared with one point six expected.

Now, the numbers are extremely small, but the risk is extremely large. If you took that as a point estimate in isolation, it would lead to fairly extraordinary risk predictions. The relative risk for lung cancer is five, the

A. (cont'd.) cumulative doses of those workers...

Q. That's what I was going to ask you.

A. ...measured in the way that they were measured in the original BOHS study, which did in fact correspond to static membrane filter samples examined in the old way, would've been of the order of a hundred fiber years.

Q. I think just so that we are all clear, because I think when you say the relative risk is five, you are there looking at the lung cancers...

A. Beyond twenty years after first exposure.

Q. Beyond twenty years after first exposure?

A. Yes.

Q. Are we all clear on that?

A. Shall I stick it on the board?

Q. I think I can clear it up.

We are looking at the lung cancer figures for those employees twenty years from first exposure, which are the figures seven plus one of the actual observed.

The next column are the expecteds. There is no actual relative risk calculation within the table.

DR. DUPRE: Yes, I think so, counsel, but just to make sure, we are looking at...at least I am looking at table one, page 830.

MR. LASKIN: Correct.

DR. DUPRE: And I assume that the discussion that is now taking place involves the numbers that all appear to the right of the words '1951 or later', because this is the updated, accurate measurement cohort. Correct?

MR. LASKIN: Correct.

DR. DUPRE: Okay.

MR. LASKIN: And...

DR. DUPRE: And after lung cancer...I'm sorry... for instance, when you said that there was an excess risk of

MR. LASKIN: I think he is going to show it to you.

DR. DUPRE: Okay. Sorry.

THE WITNESS: Beyond twenty years after first exposure, as you've seen in cohorts such as this where the risk is accumulated over a period, is where the risk starts to show up, there were eight lung cancer deaths compared with one point six expected, which is a relative risk of five.

Now, the cumulative exposures of these workers, according to the revised dust estimates, were of the order of three hundred fibers per ML years. If you look at the conversion between the old and the new figures, which is in the same table, they would have been of the order of a hundred fibers per ML years in terms of static measurements, static membrane filter measurements taken in 1961, taken 1961 to about 1974. By the technology that we used at that time for membrane filters, their cumulative doses would have been a hundred particle per ML years, which coincidentally, on the basis of the same measurements, was predicted to cause a lifelong risk of one percent...

Q. Can we just hold on so we get this in perspective? First of all, to get into your cohort you need...maybe we should make that clear...you need a minimum of ten years exposure...to get into this cohort that forms the basis for this relative risk calculation.

A. Yes. They all had to have worked for at least ten years, starting in 1951 or later.

Q. All right. Then you have looked, for the purpose of this calculation, only at persons twenty or more years since first exposure?

A. Yes, that's right.

Q. Now, the figure a hundred fibers per milliliter years, is that an average cumulative exposure for all of the group of people who met the two criteria - ten years minimum exposure, twenty or more years from first exposure?

A. Yes.

Q. That's their average?

A. Yes. You can see that from the...I mean, the original dust level estimates were back ten, twelve, ten fibers per ML in 1951, and they fell to about five by 1956.

Q. You can basically see that from table two at page 832.

A. Yes, in the original measurements. So if you started in 1951, you could have accumulated a dose of somewhere between twenty and fifty fiber years by 1955. Then a level of five for another ten or fifteen years after that would give you another fifty or so. It would give you something of the order of a hundred fiber per ML years, cumulative dose.

Q. Okay.

A. And the revision of the data increases that to three hundred fiber per ML years.

In a sense, I mean, these data are going to give you...I mean they illustrate how large these factors are and how important the questions are, because the...I mean the relative risk is five there. The total is eight over one point six expected.

So the relative risk is five.

In England, that means that half of them are going to die of lung cancer, and you can see that that's true directly, because you are looking at the total deaths beyond twenty years in that table. I think there are eight lung cancer deaths out of a total of fifteen.

Now, I think that's probably been exaggerated by chance, that observation, and it seems difficult to believe that the results can be as different in people employed after 1950, compared with people employed before, and that seems rather extraordinary. If you look at the other part of the table, the relative risk is actually significantly lower, which is

A. (cont'd.) rather difficult to explain. But..

Q. The comparable relative risk would be twenty-two over about fourteen or thirteen? The comparable calculations?

A. Yes. There's less than two for people exposed before 1950, which is very mysterious.

Q. In view of the supposedly lower dust levels?

A. Yes, quite.

Q. Do you draw any conclusions from that?

A. I don't know. I mean, the other one was a retrospective cohort study, whereas these data were collected prospectively, and this is a genuine prospective study in the sense that we established the cohort and these observations are taken since it was established. Whereas the previous one is compiled by taking company records and working backwards.

So this is, in that sense, more reliable.

That's the difficulty with these data, that in fact by any normal criteria these are...I mean, they are rotten data because of the ambiguities of measurement and so on, but they are nonetheless the best data around if you want to relate lung cancer rates to measured dust levels.

That's what worries me, that the risk estimates that they produce are actually completely inconsistent with the estimates in the Simpson Report.

Q. Can you just show us that, how those risk estimates or that risk estimate is inconsistent with the risk estimate in the Simpson Report?

A. Well, I mean, it's quite interesting to go from the original measurements that the current standard is based on, to the current situation. I mean, the original measurements...

Q. Can you take us through that slowly?

A. Yes. I mean, the measurements which correspond to the actual measured levels. I mean, everything since then is speculation, so all I've done is split them into factors and explain what has happened.

But the actual measurements correspond more or less to a hundred fiber per ML years cumulative dose in these people, so you have a hundred fiber per ML years, which equals fifty years at two fibers, of course.

Q. Right.

A. Two fibers per ML.

And you have a relative risk of five, so the excess risk...in other words, the chance of dying of lung cancer...is about forty percent in England. I mean, roughly ten percent of people die of lung cancer, and so if you increase that by a factor of five, that gives you something on the order of forty, because ten would die as a result of no exposure.

If you assume that in fact it should be three hundred, you apply these conversion factors, that would reduce the excess to something in the order of thirteen percent.

If you try and reconcile the results of this study with the previous one, they are actually inconsistent. If you take the lower...this is the fiber adjustment from one hundred equals three hundred...if you take the lower ninety-five percent confidence interval for the relative risk, which equals two point one relative of five, the actual confidence interval is from two point one to nine point seven, in fact.

Q. A ninety-five percent confidence interval?

A. Yes. Then the excess risk, the relative risk is two point one, so the excess is reduced by a factor of almost four, you see. I mean, the excess is the relative risk minus one, so the forty percent excess becomes eleven percent excess. When we've got adjustment of thirteen percent,

A. (cont'd.) it goes down to four.

So if you find that, you then estimate the lifelong excess risk as being four percent.

If you then apply the adjustment which..

Q. Can you just slow down. Can you just do that again so .....everybody else seemed to follow it, but I didn't.

A. The lower ninety-five percent confidence... the five relative risk is based on these tiny numbers.

Q. Correct.

A. So you've got no idea what it is. It's five as a point estimate, but in fact the ninety-five percent confidence interval is from two point one to nine point seven.

Q. Okay.

A. For the relative risk.

If you take the lower ninety-five percent confidence interval on the basis that it's anomalous that the risk should be so high in this study when in the same cohort it was lower in earlier workers, then you reduce that by another factor of three or so, because the excess is a third...

Q. Okay.

A. Finally, if you say, as was done in the Simpson Report, that in fact you only actually were exposed four hours a day, actually exposed four hours per day, per eight hour day, which further reduces it by a factor of two, that becomes an excess risk of two percent, corresponding to fifty years at two fibers.

The Simpson Committee said that the lung cancer risk should be more or less doubled, and I think I agree with them. They say because of asbestosis. I would have said it was more because of mesothelioma in young employees. But anyway, if you double that, it comes to four percent.

The remarkable thing is that even having applied

A. (cont'd.) all these adjustments from forty percent to two percent, none of which is clearly justified...I mean, it isn't at all clear that this fiber level adjustment is justified, the evidence is rather weak...to take the lower ninety-five percent confidence interval is very dubious, and it could be argued that when you are talking about a serious public health matter you should take the upper ninety-five percent confidence interval to be on the safe side.

I can't comment on this as to people not in fact being exposed at the ambient level for most of the working day, when you have made a series of extremely optimistic adjustments which has reduced your risk estimate by a factor of twenty, and it's still double the estimate which the Simpson Committee comes up with.

The Simpson Committee comes up with a figure of, I think...is it doubled or not? I'm not sure, actually. They finish up with...what's the figure they finally choose...that may be the figure they finish up with, actually. I think that may be the figure they finally came up with. They said one percent.

Q. Can you help us...I take it the ultimate figure you end up with is four percent, on the assumption that lung cancer deaths are accountable for half of the asbestos-related deaths?

A. Well, I mean, I'm not sure that this succession of adjustments is correct, you see. The thing is, this estimate is what would be...if anybody else did the study... this is the estimate that they would present. When other people do studies they take the observed relative risk and they try and estimate what the corresponding health measurement would be, and compute on that basis.

Q. You are giving the most favourable outlook to a lower standard, based on your calculations?

A. Yes. You can see how large the effect is, and it seems to me that this particular set of data should be looked at more carefully, because it seems to me to be rather important.

Q. Can you perhaps take the Simpson Report...I don't know whether I took it back from you or not...and just tell us how that calculation compares with what they did?

I'm sorry, I may have stolen it back from you.

A. No, there it is.

DR. DUPRE: Table thirty-six, is it, that you are directing us to, counsel? In the Simpson Report?

MR. LASKIN: I think that's the environmental slide.

DR. DUPRE: Sorry, table thirty-five.

MR. LASKIN: We are still on table thirty-five, I take it.

THE WITNESS: A. The range of predictions in table two...table thirty-seven, isn't it?

MR. LASKIN: Table thirty-five.

A. Table thirty-five, yes.

Q. Table thirty-five.

A. The major predictions in thirty-five suggest that the excess lung cancer rate will be one percent after fifty years exposure at between nought point four and five fibers per ML.

This would imply an excess risk of between two point five percent and nought point two percent at a level of one fiber per ML.

I'm not sure that it's going to help to go through this verbally, and I think I might have to have five minutes in peace to write it on the board.

MR. LASKIN: Sure. Why don't we take a break.

DR. DUPRE: Shall we take a break at this time?

THE WITNESS: Isn't it a bit premature for a break?

MR. LASKIN: No, no. I think it would be quite helpful.

THE WITNESS: This is actually quite complicated.

MR. LASKIN: I think it would be helpful to us to have it.

DR. DUPRE: So let's not take a break, is that what you are saying?

MR. LASKIN: No, I'm saying let's give Mr. Peto five minutes to work it out, and we'll take a break.

DR. DUPRE: Oh, fine.

THE WITNESS: I haven't summarized it.

THE INQUIRY RECESSED

- - - - - - - - - - - -

THE INQUIRY RESUMED

MR. LASKIN: Q. Okay, just before you carry on, just so that we get a couple of things clear, Mr. Peto, first of all what you have done is an excess risk calculation of lung cancer at a two fiber standard, looking at it from the worst point of view to produce the most, I guess, relaxed standard?

THE WITNESS: A. Yes.

Q. Now, before you tell us about what the Simpson Report did, I just want to make clear, the Rochdale calculation that is in table thirty-five in the Simpson Report is, I take it, your original mortality study that was done in 1977 and which is in tab one of your documents in front of you?

A. Yes.

Q. As I understand it from what you've told me, it is only..if we go...can we just briefly go to that so we know what is in, what we are looking at, what is in the Simpson Report in tab one?

A. I'm not even sure that it...is it a breakdown by...? Yes, sure.

Q. You divide, in your original study, you've got five different cohorts, as I understand it?

A. Yes. There is an observed over expected ratio of approximately two for lung cancer beyond twenty years.

Q. Where do we see that?

A. In table three on page 171 of tab one.

Q. Table three, 171...Men and Women First Exposed 1933 to 1950 - lung cancer, thirty over sixteen. Is that the figure?

A. Yes.

Q. The thirty figure..

A. No, actually that's the...well, if you combine the two, that thirty...

Q. Includes mesothelioma?

A. Includes five mesotheliomas. Women are included in this as well. I mean, have you got that paper that I had in the Lancet? I think it's in...

Q. It's tab three.

A. Tab three.

Q. Page 486?

A. In a way, it's better to look at that. I mean, it's...yes, okay. I mean, this paper, in fact, goes through all the sort of calculation that I'm talking about, in some detail, in that 1978 paper. It talks about these models, in fact, for lung cancer and mesothelioma.

Q. But in terms of what appears in table thirty-five for Rochdale, what raw data of yours is Dr. Acheson in the Simpson Report using for the purposes of table thirty-five?

A. If you look at page 487 of tab three, there is a section taken from it for carcinoma.

Q. Right.

A. Okay?

Q. Mmm-hmm.

A. It says that there have been fourteen lung cancers observed, six point five had been expected, which was a relative risk of about two, corresponding to a cumulative dose of the order of two hundred fiber per ML years.

Okay?

Q. Okay.

A. That's the basis of it.

Q. Okay. All right. Now, what are you going to do for us?

A. Well, I'm just going to go quickly through the calculation which I think is on page 76 of volume one of the Simpson Report. It's tricky to follow.

The thing is, the table that you referred to, table thirty-five in volume two, gives a range of excess lifelong risk due to lung cancer alone which would correspond to fifty years exposure at one fiber, based on various studies, and the highest of those is the figure ...I'm sorry...it's fiber levels which would produce a lifelong excess risk of one percent, and the highest of those is nought point four fibers.

There is also a figure of...there are figures of nought point two and nought point three fibers corresponding to different conversions for Enterline's data. For some reason they are not discussed. It's described in the text as a range of point four to five...point four being the unadjusted Rochdale data, and the five being the Quebec data with a conversion factor of five.

So in table thirty-five of volume two, fifty years exposure to give a lung cancer excess of one percent, there is a fiber range that they state is nought point four fibers per ML to five fibers per ML.

This figure is the unadjusted from the Rochdale study, which is tab three, in fact.

Q. In the...?

A. From Rochdale.

A. (cont'd.) The way that is obtained is...in fact there was a relative risk of two for lung cancer.

Q. Right. Take us through that sequence.

A. The 1933 onwards Rochdale data, there is a relative risk of two for lung cancer.

Q. That's your fourteen over six point seven five?

A. This is lung cancer only.

Q. Right.

A. For lung cancer.

There is a relative risk of two at two hundred fiber per ML years. Therefore, assuming the excess is proportional to deaths, there would be a relative risk of one point two five at fifty fiber per ML years.

Q. You get that by dividing the excess risk by four?

A. Yes. The excess is divided. That's true. That's an excess of one, if you like, so the excess is being divided by four to go from two hundred fiber years to fifty fiber per ML years.

Q. It assumes a linear dose-response relationship?

A. Yes. Since roughly ten percent of men in England die of lung cancer, a relative risk of one point two five would mean that two and a half percent, the excess if two and a half percent. Two and a half percent of men would be dying of lung cancer at one fiber.

Therefore, to calculate the fiber level which would produce an excess risk of one percent, you divide one percent by two point five, which gives you this figure here.

Okay?

Q. No, no. I think you may have lost us.

A. If point four fibers...if four fibers for fifty years produces an excess risk of one percent, okay?, point four fibers for fifty years produces an excess risk of one percent,

A. (cont'd.) then one fiber for fifty years will produce an excess risk of two and a half percent, and that's where this figure comes from.

Okay?

Q. Got that.

A. Is it okay?

Q. Yes.

A. I may need another coffee break in a minute to see if I've got it straight.

Now, the counting procedure, because with graticule counting it's supposed to increase the fiber count by two, so the calculation that is gone through on...I think on page 76, volume one, in that part of the report...the logic is roughly that if there is a factor of two for graticule counting, then the relative risk would be reduced to one point one two five.

Okay? We are talking about fifty fiber years from now onwards.

Q. Okay.

A. Those are the original data, and then this is the conversions.

So that would make it one point one two five. You would halve the excess.

Q. Okay.

A. Then if you are only exposed for four hours a day at that level, or the average level is considerably lower than the actual maximum level, then that reduces...it halves the excess again, and gives you a relative risk of one point zero six two five, which corresponds to a risk of sort of point six two five percent for lung cancer.

They then doubled that to include other causes of death. It's slightly vague, but it's going to be about right, and said therefore that fifty years at one fiber will produce a lifelong excess risk of the order of one percent or less.

A. (cont'd.) Okay? So the final calculation is that the excess risk for lung cancer is going to be...and this is the upper limit of risk, this is the highest estimate of risk in the Simpson Report...this is the highest risk estimate corresponding to one fiber per ML for fifty years.

Now, as I say, this is all based on sort of historical guesses of dust levels, and the retrospective cohort study. Finding normal criteria in the later part of the study is better both because the dust levels are measured throughout it, which they weren't in the first part, and because it was a genuine prospective study where we established the cohorts and followed them forward.

In the second part of the study, the actual observed and expected numbers, as I say, were eight over one point six expected beyond twenty years, which gives a relative risk of five. The best estimates of the original measured levels would give a cumulative dose of the order of a hundred fiber years.

As I say, if you do this...which would...hang on a minute...so in 1951 onwards study, the relative risk...this is again for lung cancer only...equals eight over one point six two, which is roughly five, at a hundred fiber years, which would be... that's an excess of four, if you like, so that would be...which would be three at fifty fiber years, to correspond to this, fifty fiber years.

Q. How do you get to that?

A. Just halving the excess. I mean, that's this relative risk minus one, which is supposed to be proportional for the risk and cumulative dose.

So it would be relative risk to the order of three.

So taking the data at face value, if the membrane filter samples are taken in the way that they were from sort of 1961 to about 1970, it would seem that a hygiene standard of one, that was applied all day long, would produce...or was taken

A. (cont'd.) as an average value...would produce a relative risk of three for lung cancer, according to these data, which would be a lifelong risk of the order of twenty percent, which is considerably higher than the half of a percent, point six of a percent, that is given as the highest possible risk estimate in the Simpson Report.

Q. In the last part you lost me when you talked about a lifelong risk. How did you get...can you just explain that? You got from three to twenty?

A. Sorry. Ten percent of men in Britain die of lung cancer, and the relative risk is fairly stable over time, therefore a relative risk of two means that ten percent excess die of lung cancer. That means that there's twenty percent rather than ten percent dying of lung cancer.

A relative risk of three means thirty percent, rather than ten percent.

So it's an excess of twenty percent. It means that of the order of twenty percent of people are dying of lung cancer as a result of exposure.

Q. What is the comparable figure, taking the calculation in the Acheson/Simpson Report?

A. Just over a half a percent.

Q. That's a lifelong risk figure?

A. Yes. It's a relative risk of one point eight six two five instead of a relative risk of three.

Q. That produces a lifelong risk of how much?

A. Point six two five percent.

Q. Rather than ...

A. Rather than twenty percent.

Q. ...twenty percent.

A. As I say, when you go through this...even if you go through this process of using the adjusted, the revised

A. (cont'd.) dust levels, which is reduced by a factor of three, taking the lower ninety-five percent confidence interval, which reduces it by a factor of about four, and then halving it for the four hours a day, to two percent, you are still well above the highest estimate of risk that is offered in the Simpson Report.

Q. I guess my next question is really, what specifically then do you take issue with...what I'm thinking of is the paper that you published in 1980 in which you did this calculation, I take it, was not available to the Simpson Report when it did its risk calculation?

A. Yes.

Q. So you say they should have used different data from the 1977 paper, and done a different calculation? I'm not sure what you are suggesting.

A. No, I don't think that the...I think that with the data that they had available, the estimates are reasonable. But..I mean, I think there were errors in the report. I think they assumed too firmly that mesothelioma isn't caused by chrysotile, and I think the weight of evidence suggests that it is.

Q. I'm going to come to that in a moment, but just sticking...

A. But as far as lung cancer goes, I think that this is reasonable. The fact that they took a range of estimates, the other end of which I think is quite unreasonable, is rather beside the point. I mean, the thing I take issue with is really a matter of presentation rather than scientific content, because they produce a range of risk estimates and this is the highest of them.

Q. The calculation...

A. If enough of this is the estimate under these conditions...I mean, assuming that this counting adjustment and

A. (cont'd.) the four hour adjustment are correct, and I can't comment on that, it depends on the way the standards are enforced.

I mean, if the standards are interpreted as being maximum which are not to be exceeded, that would be reasonable. But if they are interpreted as being averages, time weighted averages, which is what these measurements are, then it wouldn't be reasonable, of course.

I mean, there is a factor of two for a four hour day, based on the assumption that the average would in fact be, the time weighted average where people work would be considerably lower than the actual hygiene standard, and that's a matter of implementation.

But in practical terms, I mean I think that this estimate may, you know, subject to these provisos, may be reasonable. But since the further data produce a risk estimate which is very much higher...very, very much higher...as a point estimate, and more than double...even if you make a very large series of adjustments you still finish up with a higher figure from that one.

It seems to me that that estimate is wrong.

MR. LASKIN: Did you have a question? Please interject.

DR. DUPRE: Well, I was just asking my colleague whether he had joined the navy as I felt I just had. I am a little bit at sea at this point, I must confess.

DR. UFFEN: At the risk of belabouring this too long, where I got lost was when you went from relative risk of one point zero six two five. The next line..

THE WITNESS: I'm sorry. The thing is, in Britain in at the moment...

DR. UFFEN: In what?

THE WITNESS: This whole thing is predicated on the fact that the effects of asbestos multiply with smoking, and in Britain, among men, ten percent of men die of lung cancer. So a relative risk of two means that you have doubled the lung cancer risk, and therefore...

DR. UFFEN: In other words, if you wrote a little remark in there between going from that line to the next line...

THE WITNESS: Yes, I'm sorry.

DR. UFFEN: And how you got to the zero point six two percent.

THE WITNESS: I mean, ten percent, approximately, of male deaths in the U.K. are due to lung cancer. As I say, this is going to reduce in the future because there has already been a substantial adjustment in the tar level of cigarettes, and lung cancer rates are now dropping in Britain.

So in fact there is a slight revision of these data, of the order of thirty percent. But, I mean, that's not certainly a factor...therefore, a relative risk of two implies an excess of ten percent.

In other words, that ten percent of men die of lung cancer as the result of asbestos exposure. I mean, the relative risk of two implies twenty percent of deaths are due to lung cancer, which implies that there is a ten percent excess due to asbestos.

So all the way through the calculation, whatever... you subtract one from the relative risk and multiply by ten percent to halve the excess risk, basically. So that if you've got a relative risk of three, that implies that there is a twenty percent excess.

DR. UFFEN: Would you like to write that down? Subtract one from the relative risk...and multiply by...

THE WITNESS: Yes, the excess risk for lung cancer is roughly equal to the relative risk minus one, times ten percent.

THE WITNESS: (contd.) That's true all the way through, so a relative risk of three means twenty percent, so on and so forth.

MR. LASKIN: Q. I don't know whether I'm complicating it, but I find it of some assistance to look at table twenty-four A in the Simpson Report, which...

THE WITNESS: A. This is a subset of the other table.

Q. Redone.

A. Yes.

Q. And it seems to me that that helps to show, to put the excesses in some perspective.

Does everybody have table twenty-four A...

A. Yes, table twenty-four A on page 77, volume one of the Simpson Report.

Q. That I take it, Mr. Peto, does show that the Rochdale data taken on their face produce the highest excess mortality calculation from lung cancer?

A. Yes. In fact, I mean, that links up. If you look at the title, whatever it is, the paper I had in the Lancet in 1978, which was in fact a submission to the Simpson Committee, that calculates a lifelong risk due to lung cancer of the order of five percent. I think the figure is actually four percent, but it's a lifelong risk of that order, associated with a two fiber standard.

Q. Okay. What...I take it that another way of looking at table twenty-four A is to say...another way of looking at the calculation is that the Simpson Report took table twenty-four A and made two further assumptions - number one: the counting method, and number two: the average exposure would be not eight hours a day, but four hours a day, and therefore calculated a range of excess mortality which had its high end your Rochdale data, and which had its low end...I take it...the Quebec data?

A. Yes.

Q. And felt that somehow in the milieu of the average of that range that the one fiber standard seemed acceptable.

A. Yes.

Q. I take it that one of your comments is that, given what you've said about the other studies and the Rochdale study, that perhaps they ought to have focussed on the Rochdale data and looked at it more particularly?

A. Well, certainly for textile workers. I mean, I think it's a question of whether you can expect the same relationships to be found under other industries. It's a difficult one, because it seems that...it seems quite likely that textile processing produces finer fibers and carries a high risk.

As I say, it would be absurd to assume that these predictions should be applied directly to Canadian miners. Because the evidence just doesn't support it.

Q. How far do you take that? Do you take that as far as to suggest that one should be looking at regulating different industries differently, within the asbestos industry in general?

A. I don't know. I'm sorry that I can't ask questions of the audience, because I don't know to what extent fiber dimensions have been looked at in different industries, and particularly in mining.

I think that these....I mean, I 'm sure that the better studies would show some substantial differences in the fiber length and thickness which would make these apparent anomalies less anomalous.

Q. So just to sum up what your view of this risk assessment in table thirty-five and then at page 76 of the Simpson Report, I take it you accept the fact that they didn't have the updated mortality data that you have shown in 1980?

A. Yes.

Q. They really only had the data that was available to them.

A. Yes.

Q. But what you are attempting to demonstrate is that, first of all the way they presented it, you have some concern with that, and secondly, perhaps their failure to specifically look at Rochdale, especially for the textile industry, and to take into account mining and whatever else when they did the calculation?

A. Yes. It's peculiarly anomalous, because it is actually, as I say, it is the factory that was selected as being the basis of the current legislation on asbestos. It would seem an appropriate place to go on looking, unless you can find a data set that is demonstrably better.

It seems to me that the other ones that they used would be worse.

Q. Can we turn to your second...

DR. MUSTARD: John?

MR. LASKIN: Yes. I'm sorry, Dr. Mustard.

DR. MUSTARD: Before you...you are switching the subject now, are you?

MR. LASKIN: Yes, but by all means carry on.

DR. MUSTARD: Well, it would help me if you would clarify whether, in table five at tab ten, which is your lung cancer excess risk calculation that you handed out today...

THE WITNESS: Oh, yes.

DR. MUSTARD: Where you have that one fiber per ML for six years, whether that calculation is based on the assumptions that you have been showing us, the revised dust figures?

THE WITNESS: No, I think I used the estimates and excesses in relation to the U.S. insulators in that.

THE WITNESS: (cont'd.) That was meant to be illustrative rather than definitive. I mean, that was to illustrate the methodology rather than to produce results.

DR. MUSTARD: Do you know what impact on this calculation would be created by using those assumptions that you have just described for us?

THE WITNESS: It wouldn't change them grossly.

Yes, it was based on the assumption that the relative risk of six was produced by cumulative dose of six hundred fiber years, and...

DR. MUSTARD: We have fifty fiber years.

THE WITNESS: The calculation on the Simpson Report is based on an excess of one or two hundred, which would be...sorry, two at two hundred would be four at six hundred, and the excess would be multiplied by three. So it's quite comparable, in fact. It's comparable. Those calculations are comparable to the data based on the original Rochdale study, and comparable to those figures.

If these figures are correct, that would tend to increase these numbers.

DR. MUSTARD: By a factor of about three?

THE WITNESS: Well, it depends which part of that column for forty percent to two percent you choose to use.

I must say in relation to schools...I mean, my understanding is that the fibers that are found in those sort of circumstances are less likely to be dangerous. I mean, I think that the fibers that are counted tend not to be very long ones, which are thought to be the most dangerous ones.

So I think that estimates of risk of that sort, if anything, would be exaggerated in that sort of context.

I'm not sure of that, but I think that's true.

But in any case, the actual calculated risks are very low, so I mean ...the actual fiber measurements are what

THE WITNESS: (cont'd.) they are and public buildings tend to be low.

MR. LASKIN: Q. Can I ask you this one other question on all this calculation? Are you also suggesting that the Simpson Committee or Dr. Acheson should have put confidence intervals on their risk assessments, in the same way that you did when you made your calculation?

THE WITNESS: A. I don't know really. I mean, in a sense it isn't the point. As you can see, the errors in these calculations are literally orders of magnitude.

Q. Exactly.

A. So in a sense, whether the confidence limit.. if you are wrong by a factor of three or four, there is a statistical fluctuation.

In other words, if the death rate is four percent rather than one percent or point two five percent, it doesn't really add up to a row of beans because the errors in the assumptions that you are introducing are larger than that.

I mean, it is an extraordinary situation. I don't know...I can't answer that question. I don't think it would be reasonable to legislate on the most pessimistic possible assumption, because there could hardly be one.

Nor do I think it's reasonable to legislate on the most optimistic assumption.

Q. Is that what you suggest that was done in the Simpson Report?

A. Not really, no. I mean, as I say, those are calculations based on the Rochdale data, which did produce the highest risk estimates anyway, and the later study wasn't available at that time.

Q. The reason I'm just trying to inquire is the reason you put confidence intervals, and I take it it was just to demonstrate the point that even on one view of the

Q. (cont'd.) situation you still produce a figure that is several magnitudes higher than the figure in the Simpson Report?

A. Well, I mean the numbers are extremely small. I think we ought to emphasize how small they are.

Q. Fair enough.

A. It's useful to point out that they are as big as that.

But I mean, the actual estimated excess changes by a factor of three or four purely as a result of fluctuations, leaving everything else aside in that calculation.

Q. Let's turn to the second point that you made, which was your conclusion that chrysotile has rarely caused mesothelioma, and the Simpson Report ignored this disease in the risk assessment calculations.

I know you have spoken about that to some extent this morning, but could you perhaps elaborate again now?

A. Broadly speaking, as I say, with the notable exception of that one study by Rossiter in the English dockyard, which is in the Lyon proceedings, the ratio of mesothelioma to excess...pleural mesotheliom...to excess lung cancer is more or less the same irrespective of what you are exposed to.

I mean, there aren't large differences between different fiber types.

So for example, there is a fundamental illogicality in the assumption that is really quite explicit in the Simpson Report, that mesotheliomas which had occurred at Rochdale had been due to relatively minor contamination by crocidolite.

Since in people exposed to crocidolite the ratio of lung cancer to mesothelioma...excess lung cancer to mesothelioma... is more or less the same as it is in other cohorts, it would be... well, you would in fact be obliged, if you accepted that hypothesis,

A. (cont'd.) to assume that all the lung cancers are also due to the minimal contamination of crocidolite, and to ignore all excesses in chrysotile population. Since you observed crocidolite miners and find that their excess lung cancer to mesothelioma ratio is more or less the same as that observed at Rochdale, or for that observed in the Canadian mines for that matter, I can't imagine there is a great deal of crocidolite in Canadian mines, Canadian chrysotile mines, but it would be logical to ignore all excesses of cancer in any situation where there had been any crocidolite at all, if you follow the logic on that...which they didn't do.

It seems to me that you've got to look at it more formally. As I said, when you find that the ratio is more or less the same irrespective of what people are exposed to, and in particular when you find that the absolute incidence of pleural mesothelioma is very much the same in situations where there was very little crocidolite, certainly, as it was in populations that had been very heavily exposed to crocidolite, it seems to me very unlikely that those mesotheliomas have been caused by crocidolite.

On top of that, of course, there is the animal evidence that it's fiber dimension rather than type that matters, and in fact that chrysotile is at least as likely to cause mesothelioma as crocidolite.

And finally, the evidence that chrysotile migrates preferentially to the pleura, that if you look at the lung samples, if you look at the lung parenchyma, you find virtually no chrysotile. Chrysotile disappears from the lung parenchyma.

Most of the studies, the lung tissue studies, that have been done in England, are really not of much value for that reason, because Sebastien and the group in France have shown...they showed five years ago that you get a preferential migration with chrysotile to the pleura, and that if

A. (cont'd.) you look at the ratio of chrysotile to crocidolite, you find that the high ratio in the pleura, you find an excess of chrysotile to amphibole in the pleura, and a virtual absence of chrysotile in the lung parenchyma.

Q. In mesothelioma patients at autopsy?

A. Yes. In general, but in particular in mesothelioma patients.

That's on page 237 in volune one of the proceedings of the...

Q. The Lyon conference?

A. The Lyon conference, yes, on page 237 there is a paper by Sebastien, Johnson and Gaudechez, and they show in that paper that the fiber concentrations of asbestos in the lung parenchyma and the parietal pleura are virtually uncorrelated. I think, I'm not sure if it's in this paper or another one, that the...oh, yes...on page 240, figure two of that paper, there is a graph which shows the percentage of fibers which are chrysotile type, and found in the lung and the pleura, and in the lung they vary continuously from sort of nought to a hundred percent. Whereas the great majority of fibers found in the pleura are in fact chrysotile.

So if anything, I mean the animal evidence and the physiological evidence would tend to suggest that chrysotile is more, rather than less, likely to cause pleural mesotheliomas than crocidolite.

I don't think that's the case, because as I said, the epidemiology suggests that they are more or less the same, but to assume quite firmly that it doesn't seems to me unreasonable on the basis of the evidence available.

Q. Assuming...

A. I should add that in fact that's a view which is generally held in the States. I mean, it's a peculiarly English interpretation perhaps because our asbestos industry is

A. (cont'd.) more devoted to chrysotile than yours is. I mean, most people, I think, in America, would agree with that interpretation.

Q. The view that you have put forward?

A. Yes.

Q. Taking your point for the moment, how then can you then tell us how mesotheliomas should have been included in the risk assessment that the Simpson Committee made?

A. In the way that I did in that...in tab three. I mean, that paper in the Lancet. That aspect of it was ignored in the Simpson Report, but if you look at the footnote on page 484, you will find that this was a report presented to the Advisory Committee on Asbestos, June 28, 1977.

Q. Tab three, which is before us then, was, in essentially this form, submitted to the Simpson Committee?

A. Yes.

Q. As you say, essentially ignored by them?

A. That aspect of it was, yes.

Q. Where do we find the manner in which you took mesothelioma into consideration?

A. There is a section on page 487. I would not suggest that this paper, in itself...the methodology is appropriate, but I think the data that I showed this morning which shows that the ratio of mesothelioma to lung cancer in virtually every substantial cohort study is more or less the same. I mean, this was based on five cases, when I wrote this. That's how many cases we had in the cohort at that time.

I mean the fact that the models that I suggested in this paper are borne out in great detail by the two hundred and thirty-five cases which, among American insulators, and the consistency with the other studies that are reviewed in whatever paper it is, tab ten or whatever it is, I mean, I think that the evidence that this is an appropriate way of analyzing

A. (cont'.d) it is rather strong there.

Q. Your conclusion at the top of page 488 was that there was a lifelong attributable risk to a person exposed to one fiber per cubic centimeter of approximately two percent?

A. Yes, that's certainly approximately correct. I think it may be slightly too high, but I would need to recalculate it on the basis of the other studies that have become available since then. It's of that order.

Q. So...and does that figure, given the caveats that you, yourself, have placed on it, but is that figure then comparable in terms of the point six two five percent figure, lifelong risk for lung cancer?

A. Well, in fact we finish up with more or less the same answer as the Simpson Report, in which they doubled the lung cancer predictions to allow for asbestosis, and I would double them to allow for asbestosis and mesothelioma combined.

Q. I see. That's what I was getting to.

A. So, I mean, that aspect of it, I think they got the right answer for the wrong reason.

But I think it is significant in terms of...it's obviously particularly significant in terms of childhood exposure, but it may also be significant in the future.

I mean, I hope that people will give up smoking in the future, and if they do, mesothelioma would be the...you know, would constitute by far the majority of deaths caused by asbestos. Both asbestosis, as well as lung cancer, is largely confined to cigarette smokers. Asbestosis mortality among asbestos workers is very much higher for cigarette smokers than nonsmokers.

Q. The ten percent background rate of lung cancer in Great Britain, which is part of that calculation that you did, is that a calculation that includes cigarette smoking?

A. Oh, yes. I mean, that's the gross rate in Great Britain. It's of the order of fifteen percent in cigarette

A. (cont'd.) smokers and, fifteen to twenty percent in cigarette smokers, and virtually zero in nonsmokers.

Q. Could you update us yourself as to what the...

A. I say virtually zero. I mean, it's very much lower, less than one percent among nonsmokers.

Q. What is the present...looking back over time... what, up to the present, is the mesothelioma experience in your Rochdale cohort?

A. In our cohort...well, it's described in that paper in the Lyon meeting. There were, I think, a total of fourteen cases, including a cohort of people who were exposed before 1930.

I mean, it isn't useful from that point of view. It's too small.

Q. But as I understand it, the cohort that you looked at for your mortality studies, which varied between a thousand and down to seven hundred people, I take it is only a small part of the total number of employees at Rochdale...

A. Yes.

Q. ...over the years?

A. Yes, that's right.

Q. I think you told me that there were thirty-five thousand employees at Rochdale in the complete number?

A. Yes.

Q. Can you tell us...what I'm looking at really is your tab three, on page 488, where you discuss brief or nonoccupational exposure.

A. Yes.

Q. I note that up to the end of 1975, you say there have been ten cases of pleural mesothelioma among approximately twenty thousand men first employed in the factory after 1933.

A. Yes. The majority of the cases, in fact,

A. (cont'd.) were employed before that time, the majority of them had been employed before 1930, so they were really of no value at all from the point of view of risk estimation.

So, I mean, I think it's only since 1933 that the employment records are reliable and one has any idea of what sort of exposures people had.

It's interesting that all of them have been pleural, though. I don't think there is a single peritoneal mesothelioma among more than forty cases, I think.

Q. Is it still true, as you indicated at page 488, that only one of those cases occurred in those persons employed for less than two years?

A. I think that's still true, yes. I haven't... can you give me that page of the study?

Q. Tab three, page 488.

A. I think that's worth mentioning. I don't think there is any evidence...in fact, I think all the evidence goes the other way. I think that the minimal exposure is disproportionately dangerous. I mean, there are anecdotes of people exposed to asbestos one day and got mesothelioma, and I think the study that we did in Los Angeles...and studies that other people have done...studies by Alison McDonald done in the U.S. and in Canada...show quite clearly that there are mesotheliomas occurring in people, which are apparently not due to asbestos. I mean, there were mesotheliomas in people who don't have heavy lung dusts, and absolutely no history of exposure to asbestos.

To assume on the basis of anecdotes that people who drilled a hole in an asbestos roof when they were twenty, who get mesotheliomas fifty years later due to that exposure, I think it's completely unreasonable. I think it's very unlikely that the effect of brief exposure is more than proportional,

A. (cont'd.) and the majority of cases seem to be occurring in people who have had fairly substantial exposure.

Q. Are you suggesting then that there are other factors which we may, or other substances which we may not yet have been able to identify, which are in some cases responsible for the mesotheliomas?

A. I would guess that it's a natural disease. I would guess...I mean, just as lung cancer is a disease that people get spontaneously, I would guess that mesothelioma is a disease that people get spontaneously. But I mean, it is difficult to be sure.

But as I say, the fact that the age distribution of unexposed cases is so different, and the fact that the incidence is more or less the same in men as in women, suggests that it's simply a spontaneous cancer.

Q. In your Los Angeles study, where I take it you found a substantial number of people who had mesothelioma for whom you could not attribute an asbestos exposure, did you or your group make any further inquiries to see if you could ascertain what may have been the cause of the mesothelioma?

A. No. I mean, the majority of interviews weren't with the cases. Obviously the cases had died, and the majority of interviews were with next of kin.

There were a number of cases where you couldn't get satisfactory information and we simply excluded them from the analysis. The fifty-five, there was as definite a statement as you can get from a next of kin, that there had been no exposure.

Q. Fifty-five cases of mesothelioma?

A. There were fifty-five cases in...that's, as I said, that's not reported in the paper. I've got only forty-one in the paper that I presented, because those are 1974 to 1978 cases, but in fact including the 1972, 1973 and 1979 cases, there were fifty-five.

Q. I just want to understand this. In your study of Los Angeles County, you...

A. There were fifty-five out of a hundred and eighty-eight cases that were initially interviewed, who were reported as having no exposure to asbestos.

DR. DUPRE: Counsel, could I go back to the original question that started this latest part of the dialogue, which, as I recall it, dealt with the number of mesotheliomas found in the Rochdale cohort.

One answer that came back, if I recall correctly, was forty?

THE WITNESS: I don't know the exact number, but there have been more than forty all together. That was given as evidence by Turner in New Orleans, back to the English Advisory Committee.

DR. DUPRE: The main source of my confusion is whether we are looking at the Rochdale 1933 cohort, as I will call it...

THE WITNESS: No, no. No, these are people who have worked in that factory, or certain other factories, and as I say, the majority of them in fact had been exposed prior to 1933, and the employment records are so incomplete that it's really very difficult to do any sort of useful epidemiological analysis of them.

DR. DUPRE: What about the Rochdale cohort that is post-1951, with ten or more years of employment. Am I correct in remembering that cohort...

THE WITNESS: Yes.

DR. DUPRE: ...with that description?

THE WITNESS: Yes.

DR. DUPRE: How many mesotheliomas have materialized in that cohort, the 1951 with ten years of exposure?

THE WITNESS: Up to the time of the last

THE WITNESS: (cont'd.) followup, there hadn't been any.

There is a calculation in that paper, if I can find it...yes, on page 831 of tab seven.

DR. DUPRE: Tab seven. Page?

THE WITNESS: Page 831.

DR. DUPRE: Page 831.

THE WITNESS: It points out that there haven't been any cases so far, but in fact applying the incidence rates that were observed in successive five year periods since first exposure, only nought point four cases would have been expected. So the fact that none had occurred would not have been very significant. The followup is too short.

In fact, there is...I happen to know that there is one case diagnosed a month ago, in among those first exposed in 1959. I heard about that anecdotally. I doubt if there is... well, in fact I would be very surprised if there has been a mesothelioma death, because we get death certificates routinely fairly quickly.

As I say, one in fact has been diagnosed.

DR. DUPRE: So there is now, the first case, apparently, has been diagnosed in the cohort...

THE WITNESS: I'm very reluctant to put this on the record, because I discovered this personally and the man is still alive.

DR. DUPRE: But this is in the cohort of 1951 employees...

THE WITNESS: Yes.

DR. DUPRE: ...with ten or more years of exposure.

MR. LASKIN: Q. Can I ask you, accepting that there is apparently some divergence of opinion as to the amount of crocidolite that may have been used at Rochdale over the years, is there any consensus as to the time period when it was used,

Q. (cont'd.) if at all? I mean, can we isolate a time period when only chrysotile was used?

A. No. I mean, the evidence is completely anecdotal. When the cohort was first established we were told that no crocidolite had been used there, and then that information has been revised successively. You will see in the footnotes to the Simpson Report, I mean anecdotal remarks by Dr. Gilson, I think...

Q. Yes. I'm looking at the footnote on page twenty-six of Dr. Acheson's report. So it's...

A. Yes. I mean, the information is completely anecdotal. The estimates that are used in that vary from sort of virtually nothing to hundreds of tons, and I think possibly more recently. As I say, it's a very small proportion of the fiber that was used, but I mean quantities are said now to have been substantial and it's difficult to know how to verify it.

Q. Has anyone inquired into the corporate records as to whether there were imports of crocidolite?

A. Not as far as I know.

As I say though, I think the best evidence that chrysotile causes mesothelioma comes from the Canadian chrysotile mines rather than the work in Rochdale.

Q. Just one further question on your Los Angeles study. Have there been any autopsies done on the lung tissues of those persons for whom the next of kin could attribute no asbestos exposure, in the mesotheliomas?

A. Yes. That's an interesting paper. In fact the...it's not autopsies, it's pathological review of the material, and it seems that the diagnosis of mesothelioma is being queried in a substantial proporition of them.

I haven't seen any detailed data on it yet, but

A. (cont'd.) it seems...it's difficult to interpret. Unfortunately, the review wasn't done blind, so it's impossible to be sure whether or not the fact that someone was known not to have been exposed to asbestos, or that their lung didn't contain asbestos fibers, influenced the pathologist, and the study was actually arranged in a rather unsatisfactory way.

As you probably know, there is a considerable divergence between pathologists. I mean, even UICC experts sometimes range from the A coding, which means certain mesothelioma, to the E coding, which means certainly not.

The issue of mesothelioma in people not exposed to asbestos I think is an open one, and I wouldn't like to draw any firm conclusions about it. As I say, it isn't particularly relevant for your purposes, and I think it's sort of a scientific question which isn't really resolved, what proportion of them are genuinely mesothelioma.

Q. I wonder if there are just two other points you could clarify for me in respect to your last mortality study, the 1980 paper at tab seven? The first one is, could you just clarify and explain the table which is table three at the bottom of page 832?

A. Yes. This was a comparison of nominal exposures of the...the estimated exposures of the people who died of lung cancer, the eight cases who died of lung cancer. These are sort of people of comparable age, comparable exposure histories.

Q. These are the eight people with ten years or more exposure...

A. Yes.

Q. Twenty or more years time since first exposure?

A. Yes.

Q. Okay.

A. As you can see, there is no relationship at all apparently. There is no difference in the cases and controls. This is something which happens more often than most people realize, in studies of this sort, and the reason for it is obscure.

I mean, the apparently very good correlations between relative risk and cumulative dose that I showed in those data by McDonald and from Enterline, and also the data relating morbidity to cumulative dose which Geoff Berry analyzed, I suspect largely reflect the correlation between duration of exposure and risk, because duration of exposure is measured extremely accurately. So to take an extreme example, if you had absolutely uniform conditions in a factory, then certain people would, at random, develop disease, and certain people wouldn't...just as not all smokers who smoke the same amount get lung cancer.

If you did an analysis of this sort, you would find no relationship between exposure level and risk, in the sense that people who got it would be no different from those who didn't.

But at the same time, if there was variation in duration of exposure, you would find a strong relationship between risk and duration of exposure. I think that a combination of the relative heterogeneity of the cohort, and the poorness of the measurements, means that you find strong relationships between duration and risk, and very weak relationships between estimated dust level and risk.

In fact, there have been very few studies that have found good relationships between estimated dust levels and risk.

Geoff Berry mentioned...I think it's at...I think in the British Journal of Industrial Medicine paper...that the relationships that he had found were very largely expected

A. (cont;d.) in terms of correlations between risk and duration of exposure.

Q. Were very largely...sorry?

A. Due to the relationship between risk and duration of exposure.

Q. Which in most cases, I take it, is equivalent to length of employment?

A. Yes. Yes.

That people have very rarely looked at their data this way, people have very rarely taken people with comparable periods of employment over the same period and tried to relate their estimated exposure levels to their risk. When they do, they usually find rather a weak relationship.

I don't know how to interpret that. I mean, it may be that the wrong things are being measured. It may be fairly likely that you can get pretty poor estimates of individual risk when you try and do the sort of historical reconstruction.

Q. Apart from interpreting it, is there any way in which you can utilize the kinds of correlations you get between duration of exposure, length of employment and risk and a risk assessment? Can you use the nonquantitative...when I say nonquantitative I mean nonfiber-measured dose-response relationships to make any kind of risk assessment?

A. What do you mean by risk assessment?

Obviously, if you don't know what the dust levels are, you can't begin to frame a hygiene standard. But if you know what the average levels are and you assume the effect is linear, then obviously you can relate duration of exposure...which is exactly what was being done in those graphs that I showed you. You can find that there is or isn't a linear relationship between risk and duration of employment.

A. (cont'd.) And roughly speaking, there is. I mean, both for mesothelioma and for lung cancer.

Q. I take it basically, in terms of your Rochdale cohort, you have basically taken average exposures and that...

A. Yes.

Q. Rather than, you haven't assigned an individual exposure profile for each individual employee in your cohort?

A. No. I've taken those figures on page 832, the same page as the table you just referred to, weighted averages. I mean, individual estimates were obtained and then the average was calculated by just weighting by the number of people exposed at different levels.

Q. Could you just go over that again?

A. Those figures in table two on page 832 of tab seven, are averages for all the people in the group who were employed at that time.

Q. In other words, you...did you then calculate each individual's exposure in a particular year at...

A. I never had those data. As I say, Geoff Berry held the data because at that time he was doing the second BOHS study, which was in fact never published. That was the source of the original data. He simply calculated the mean, estimated the means of the estimated individual exposures in each year.

The estimates which the bottom line is based on were individual estimates which I had, which I got as a result of the revision, the new revision which increased the estimated dose by a factor of three or so, which produced the bottom row in table two. I had those data from the reconstituted BOHS Committee.

I suppose you could say the fact that they are unrelated to lung cancer risk implies that they are not very good estimates. They haven't yet been correlated with the

A. (cont'd.) morbidity, either. If they have, I haven't seen the results.

Q. In light of your earlier comment about the good relationship between duration of exposure and risk, are you suggesting that perhaps cumulative exposure measured in terms of dust or fibers or whatever may not be the most appropriate measure of dose when one is looking at dose-response relationships?

A. No. As I say, I think you have to have different models for different diseases. I think cumulative dose is all right for lung cancer, but not for mesothelioma.

I don't think that you can do better in general than getting a weighted average of exposure levels in a factory and assuming linear dose response. I don't think you would expect to get good enough measurements of individual exposure.

You can show quantitative dose response. The study by Newhouse and Berry, for example, showed that people who were very severely exposed had higher mesothelioma rates than those who were lightly exposed. You can show gross differences of that sort, but when you are talking about relatively small variations in dust levels, I think it's probably true in general that you don't find a good correlation between those estimates and the actual individual risks at a given duration of exposure.

Apparently-good relationships have usually been because you are confusing duration of exposure and the estimates of dust level.

MR. LASKIN: I was going to switch topics, but I'm happy if the Commissioners have any questions...

DR. UFFEN: I suspect my question is stupid...

MR. LASKIN: I doubt it.

DR. UFFEN: I won't be offended if you say so.

On page 832, table two that we have been talking about, there is the comment, "weighted by the number of men

DR. UFFEN: (cont'd.) at each level", and I'm not sure that I understand what that means.

THE WITNESS: It's just the average, literally. It's the average for the people in the cohort. It's the average dust level for the people in the cohort.

DR. DUPRE: Taking into account different dust levels of different jobs?

THE WITNESS: Yes. There were dust levels for each job. It was just weighted according to the number of people in the cohort.

DR. UFFEN: Weight sometimes implies that you have a little extra factor thrown in there that involves some other judgement. Average, I understand.

THE WITNESS: It was the average...it was given... I mean, if half the factory had been at twenty fibers and half at ten fibers, but all the blokes had been working in the ten fiber bit, then the weighted average would be ten.

Actually, that's the idea.

As I say, in fact that's the reason for the marginal fluctuations in there from 1936 to 1941, when the estimates in different areas didn't in fact change.

MR. LASKIN: Q. The only other topic I really wanted to cover with you concerns some of the other cohort studies that we have heard evidence about in these proceedings already, and as you might imagine, this Commission sitting here has to make some assessment of all of the various studies. We have had the benefit of your comments already with respect to some of those studies, and I wonder if you could bear with us a little longer and give us the benefit of your judgement on some of the other cohort studies?

Can I ask you, first of all, can we take...and I don't know whether you have had a chance to look at it, and if you haven't tell me so...but can we take the Dement study first

MR. LASKIN: Q. (cont'd.) of all?

THE WITNESS: A. Well, I mean it suffers from the defect that the other studies suffer from, that in fact most of excess mortality is in people who were first exposed in the thirties or forties, when no reliable measurements were taken, when measurements which can only be converted to fibers on the basis of rather speculative conversion were available.

I mean, it starts off by saying that there were five thousand, nine hundred and fifty-two dust measurements taken, but only a hundred and ninety-three of them were taken before 1945, and that's a period in which the exposure which is accounting for a good deal of the excess mortality occurred.

Q. Any other comments on that particular study?

A. Well, I had one particular query in relation to it, but I don't know whether this is a proper place to raise it. I mean, it was a technical point. I thought there was a possible error in one of the tables, but I'm not sure that one ought to raise things like this in this context.

Q. We are happy to hear about it.

A. Well, I don't even know what...the version that I've got is an old version. Can I show you a newer version?

Q. Sure. Let me show you what has now become exhibit four in our proceedings, let me put it in front of you. You've no doubt got the doctoral thesis.

A. Yes. The expected number of deaths between a hundred and two hundred thousand fiber per c.c days, in table seven, is three point four two for all causes of death, and nought point nought four for lung cancer, which means that the death rate for lung cancer, averaged over the period and age groups that were being studied, must have been roughly a hundred the death rate for all causes. I don't think there has been a period in the last thirty years in the United States when the death rate for lung cancer is a hundred of the death

A. (cont'd.) rate for all causes.

Q. Could you just go over that once again?

A. In the bottom row of that table, which is a calculation referring to mortality...

Q. Table seven?

A. Table seven...there is a row that refers to mortality for all causes, an expected number of three point four two.

Q. For the cumulative dose of...?

A. Of a hundred thousand to two hundred thousand fiber per c.c. days.

Is it three point four two?

Q. Three point four two.

A. Yes. The expected, and the expected number for lung cancer is nought point nought four, which is roughly a hundredth three point four two, and I don't think that the death rate for lung cancer among American men has been a hundredth of the death rate for all causes, in the last thirty years.

So there is something anomalous about that. I mean, either that calculation is based on a very early period among people over the age of eighty-five, or there is an error.

I don't know. It certainly isn't the result of recent death rates.

Q. One other...

A. The major difficulty with that study, as I say, is that the...like all the studies, and the Rochdale study...the exposure estimates are very doubtful, and the inconsistencies that appear to exist between different studies are very much less in terms of factors than the uncertainties that exist within all of them.

Q. One other study that we heard some evidence on yesterday concerned a study in our own jurisdiction at a plant in part of Toronto, and it concerned some papers by Dr.

Q. (cont'd.) Finkelstein, and I know you've had the papers and I don't know whether we've given you the benefit of enough time to review them to enable you to make any comments on them, but certainly if you do have any comments, we would welcome it.

A. I think it's a study which produces results comparable to the Rochdale study in fact. I mean, the same reservations about the conversion between one method of exposure measurement and another will obviously apply.

This is the one absolutely major difficulty with all studies that the committee has to review. I mean, I don't know what the solution to it is.

Q. The dust estimates?

A. Yes. I mean, how you convert, how you estimate dust estimates in the past and how you convert them one method to another is absolutely critical and completely ambiguous.

Q. When you say the results are comparable to the results at Rochdale, can you elaborate on that?

A. Well, I haven't looked at it in detail, but I think the specific risk estimates are of the same order of magnitude in relation to the relative risk for lung cancer.

DR. FINKELSTEIN: Yes, there is a factor of eight at a hundred fiber years.

THE WITNESS: A. But I mean there is a tendency which epidemiologists suffer from just as much as politicians, which is to think that people who get the same answer as you are right and everybody else is wrong.

MR. LASKIN: Q. Can I ask you specifically about the formula that Dr. Finkelstein used to make his risk calculation, and maybe I can put in front of you.

Don't at all feel rushed, Mr. Peto, because we are happy to give you some time to look at it.

A. As I understand it, aren't the models that you are using very much the same as the ones that I was presenting?

DR. FINKELSTEIN: Exactly.

THE WITNESS: In that case, I agree with them.

MR. LASKIN: Q. From what I have heard, from the way I have heard you describe your approach this morning, and indeed this afternoon, it appeared to me, in any event, that the formula that appears in Dr. Finkelstein's work is really consistent with the kind of risk assessment formulae that you put up on the board.

THE WITNESS: A. It is. So that it is or it isn't?

Q. It seemed to me that it was, but I ask the question to you.

A. That it is. I think it is, but I haven't had time to look through it in detail.

DR. DUPRE: Counsel, might I ask the following: I for one am certainly interested in Mr. Peto's judgement here, and if we are at the conclusion of your direct examination, perhaps if other parties would yield the first ten minutes at nine o'clock so that you can conclude this matter with Mr. Peto, and this would give you some time this evening, sir, to just take a quick look at the passages that Mr. Laskin is asking about.

Would that be all right?

THE WITNESS: Yes, but I'm not sure that there is very much that I can say about them, because I think that this analysis is along exactly the same lines as the one that I did, and the issue here isn't over the model fitting, but as with all the cohorts, how reliable the conversion from earlier measurements to model measurements is.

I think the apparent inconsistencies are probably less than they appear to be. I mean, you always get...Dr. Finkelstein's estimates in most estimates are, if anything, rather

THE WITNESS: (cont'd.) higher than mine.

But this hierarchy of adjustments of allowing for graticule counting and taking lower ninety-five percent confidence intervals, and so on, would be expected to reduce risks, and I don't think there is any inconsistency in terms of the results.

MR. LASKIN: Well, let me take your cue, Mr. Chairman, and subject to the Commissioners' convenience I would suggest we adjourn now and everybody is agreeable, we reconvene at nine o'clock tomorrow morning, and maybe I will steal the first five or ten minutes and then turn Mr. Peto over to my friends.

DR. DUPRE: So we shall rise then until nine o'clock?

Thank you very much, Mr. Peto. You've had a long day indeed.

We will reconvene at nine.

- - - - - - - - - - - - - - -

THE INQUIRY ADJOURNED

THE FOREGOING WAS PREPARED
FROM THE TAPED RECORDINGS
OF THE INQUIRY PROCEEDINGS

Edwina Macht

EDWINA MACHT